The Institute of Paper Chemistry

Appleton, Wisconsin

Doctor's Dissertation

The Peroxyacetic Acid Oxidation of Lignin-Related Model Compounds

William J. Lawrence

June, 1978

THE PEROXYACETIC ACID OXIDATION OF LIGNIN-RELATED MODEL COMPOUNDS

A thesis submitted by

William J. Lawrence

M.S. 1972, Lawrence University

in partial fulfillment of the requirements
of The Institute of Paper Chemistry
for the degree of Doctor of Philosophy
from Lawrence University,
Appleton, Wisconsin

June, 1978

TABLE OF CONTENTS

SUMMARY

The peroxyacetic acid oxidation of the lignin-related model compound, 1-(3,4-dimethoxyphenyl)-2-(2-methoxy-4-methylphenoxy)propanol in aqueous acetic acid at 25°C was investigated using a 5:1 molar ratio of peroxyacid to substrate. Reaction products, oxidation stoichiometry (moles peroxyacid consumed to moles substrate consumed) and half-life of this β-aryl ether in 2.5% peroxyacetic acid were determined.

The oxidation products were separated into neutral-phenolic and acidic fractions and subsequently derivatized to trimethylsilyl ethers and esters. Several of the oxidation products contained no free hydroxyl groups and were consequently analyzed as underivatized products. Gas-liquid chromatography was used for substrate and oxidation product analyses. Structural assignments of the oxidation products were made by gas chromatography-mass spectrometry and proton magnetic resonance spectrometry. Where appropriate knowns were available, additional structural proof was provided by comparison of these types of spectra and gas-liquid chromatographic retention times. All significant products detected by gas-liquid chromatography were identified. About one-third of the reacted substrate could be accounted for by the oxidation products identified. These products indicated there were at least five types of initial reaction of the β-aryl ether compound with peroxyacetic acid.

Two of these initial reactions led directly to oxidative cleavage of the β-aryl ether bond. One of these reactions led to the formation of 1-(3,4-dimethoxyphenyl)propan-1,2-diol and 4-methyl-o-benzoquinone. Due to its high reactivity, this quinone was unable to be isolated. The other β-aryl ether cleavage reaction led to the formation of 2-methoxy-4-methylphenol and 1-(3,4-dimethoxyphenyl)-1-hydroxypropan-2-one, both of which were identified as oxidation products. Investigation of the stability of the β-aryl ether to the reaction medium showed

that there was no significant amount of hydrolytic cleavage under the conditions used in this study.

A third reaction of the β-aryl ether led to side-chain displacement to give 2-(2-methoxy-4-methylphenoxy)propionaldehyde and 3,4-dimethoxyphenol. Additional proof of the aldehyde structure was provided by the identification of its reaction products, 1-(2-methoxy-4-methylphenoxy)ethyl formate and 1-(2-methoxy-4-methylphenoxy)ethyl acetate.

A fourth reaction led to oxidation of the benzylic hydroxyl to a carbonyl to give 3',4'-dimethoxy-2-(2-methoxy-4-methylphenoxy)propiophenone. While this reaction does not lead directly to cleavage of the interaryl linkage, prior work suggests subsequent Baeyer-Villiger oxidation of this ketone will lead to cleavage about the α-carbon atom of the side chain.

The fifth type of initial reaction involved demethoxylation and/or ring hydroxylation. Exact structural determination of these types of products was not possible, but the mass and proton magnetic resonance spectral data indicated that the interaryl ether linkage remained intact and that there was loss of at least one methoxyl group from the starting material.

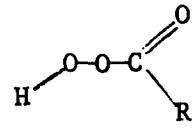
The identification of 5-carboxymethyl-4-methyl-2(5H)furanone as an oxidation product strongly suggests that oxidation of the 2-methoxy-4-methylphenoxy aromatic system to a muconic acid may occur without loss of the ring methoxyl group.

The finding of a significant number and quantity of products containing an ortho dimethoxy aromatic ring clearly shows that the first four types of reactions compete favorably with demethoxylation of the 3,4-dimethoxyphenyl aromatic structure in the β-aryl ether.

In addition, the peroxyacetic acid oxidation of 1-(3,4-dimethoxyphenyl)propan-1,2-diol and 1-(3,4-dimethoxyphenyl)-1-hydroxypropan-2-one was investigated under the same reaction conditions as the β-aryl ether model compound. The half-lives of these compounds were 60 and 1.25 hours, respectively. These half-lives reflect the expected stability of the glycol structure and the high reactivity of the carbonyl structure. While no significant amount of neutral-phenolic products were formed in the oxidation of the diol, 3,4-dimethoxyphenol accounted for approximately one-half of the oxidized α-hydroxy ketone.

INTRODUCTION

Peroxyacids form a special class of hydroperoxides in which the carbon attached to the hydroperoxy group is carbonyl as shown below:



Whereas the active oxygen in hydrogen peroxide is not readily available for many organic reactions, in peroxyacids the adjacent carbonyl sufficiently polarizes the peroxy bond as shown in Fig. 1 to form an efficient electrophilic agent. The outer oxygen atom develops a positive character and serves as the attacking point in electrophilic reactions. The reactions of peroxyacids are predominantly ionic as opposed to free radical in nature. Also shown in Fig. 1 is the existence of a particularly stable intramolecularly hydrogen bonded five-membered ring. Spectroscopic evidence has been reported for the formation of such intramolecular hydrogen bonding (1,2). The higher pK_a's of the peroxyacids compared to the corresponding carboxylic acids as shown in Table I are primarily due to the lack of a resonance-stabilized anion, but can also be attributed to the electronic polarization.

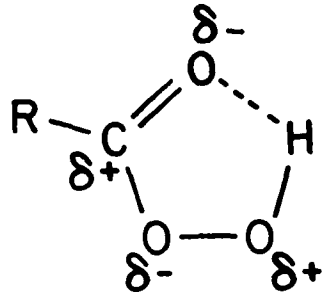


Figure 1. Polarization of Peroxycarboxylic Acids

TABLE I

pK_a VALUES OF PEROXYACIDS AND CORRESPONDING CARBOXYLIC ACIDS (3)

Acid	pK_a of Carboxylic Acid	pK_a of Peroxy Acid
$H-CO_2H$	3.6	7.1
CH_3-CO_2H	4.76	8.3
$C_6H_5-CO_2H$	4.2	7.9

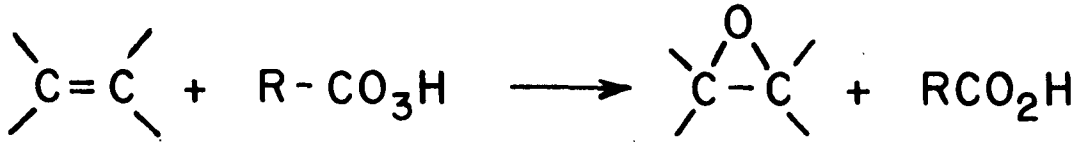
The higher incidence of electron-rich sites in the lignin (aromatic rings, carbonyl and olefinic bonds) as compared to the carbohydrate portion of wood serves as a driving force for selective delignification of wood and wood pulps with peroxyacids. In the late 1940's, Poljak first reported the use of peroxyacetic acid for delignification of wood (4). Subsequent studies have shown the efficiency of peroxyacetic acid in selective delignification of wood and wood pulp samples (5-7).

This thesis will deal with the reaction of 95% acetic acid solutions of peroxyacetic acid with a lignin-related β-aryl ether model compound and some of its oxidative products.

TYPICAL REACTIONS OF PEROXYACIDS

REACTIONS WITH OLEFINS

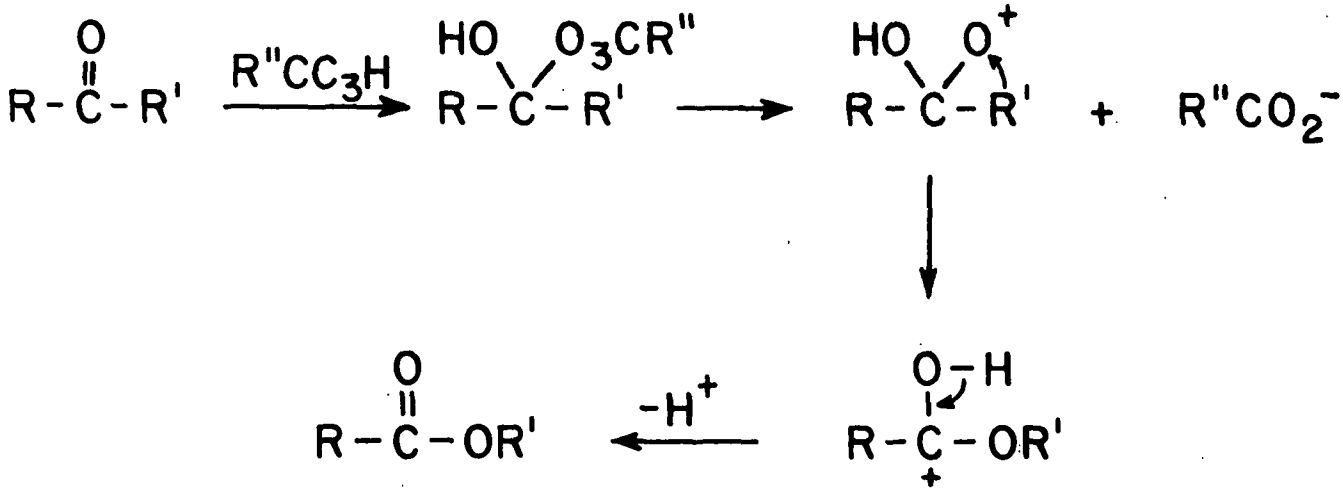
The reaction of olefins with peroxyacids has been extensively studied and several reviews have been written on this topic (3,8). The reaction involves formation of an epoxide as shown below:



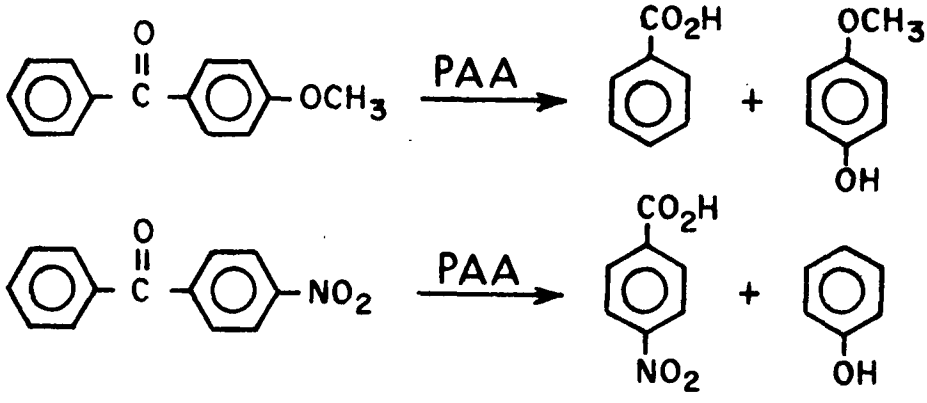
In the presence of strong acids, the epoxide ring is opened to yield α-glycols. For this reason, peroxycarboxylic acids such as peroxybenzoic acid and m-chloroperoxybenzoic acid are the reagents of choice for the isolation of epoxides because they can be isolated in high purity (95+%) easier and more safely than other common peracids. Peroxyformic and peroxyacetic acids usually contain quite high amounts of the corresponding carboxylic acids because solutions of greater than 50% purity are highly unstable and explosive (3).

REACTION WITH CARBONYL COMPOUNDS

The oxidation of ketones and aldehydes with peroxyacids via oxygen insertion is known as the Baeyer-Villiger reaction and several reviews on this reaction have appeared in the literature (9,10). The mechanism is generally agreed to be ionic in nature, acid catalyzed and follows the reaction scheme:



The substituent having the greater capability for electron release is normally the migrating group and these are in the order: tertiary alkyl > secondary alkyl > benzyl > n-alkyl > methyl (11). In the case of substituted benzophenones, the substituents affect the migrating ability of the aromatic rings according to their electron donating ability, thus the following products were formed by peroxyacetic acid oxidation (12):



In the case of alkyl-aryl ketones, the reaction is slower than that for benzophenones and can lead to benzoates or phenols (13). Similar to the benzophenones, the reactivity is increased with electron donating substituents on the aromatic ring (13).

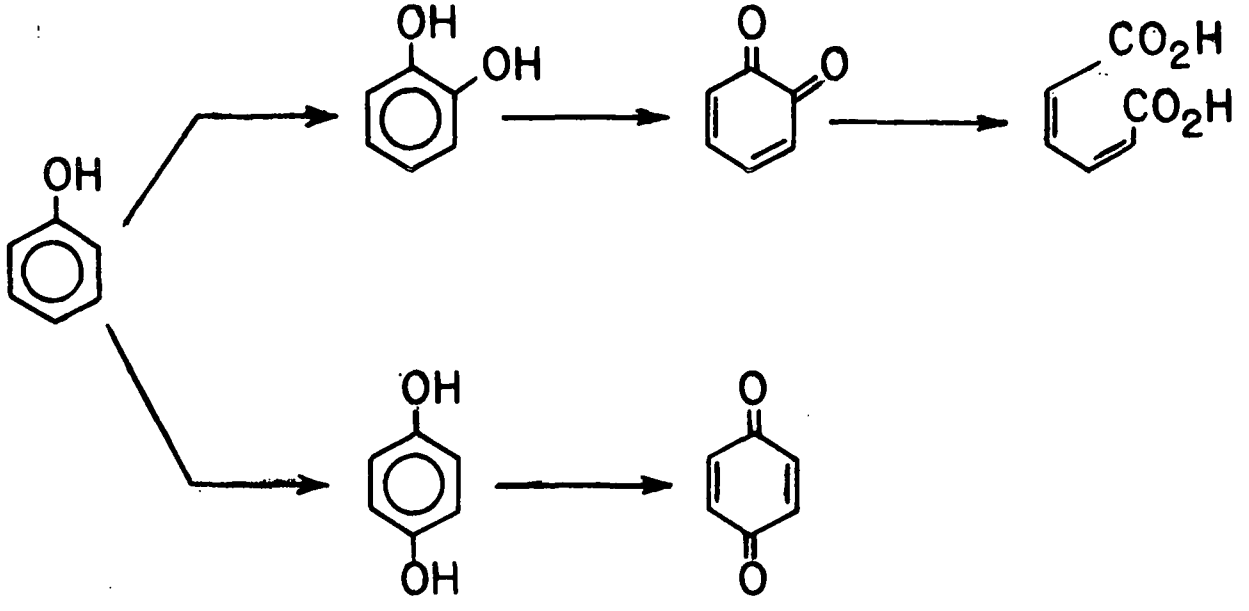
The aliphatic aldehydes usually react to form the corresponding carboxylic acids (14). Aromatic aldehydes give benzoic acids and phenols. As the strength of the electron donating properties of a substituent increases, the amount of the phenol or phenolic formate formed also increases (i.e., aryl migration).

α-Diketones undergo reaction with insertion of the oxygen between the two carbonyl groups (15). Depending on the solvent, anhydrides or carboxylic acids are obtained as products.

ELECTROPHILIC AROMATIC SUBSTITUTION

Due to the importance of the aromatic ring systems in the structure of lignin, perhaps the most important reaction of peroxyacetic acid with lignin is electrophilic aromatic substitution. This type of reaction has been shown to have large negative reaction constants, Hammett ρ values, on the order of -4 to -12 (16). Negative ρ values indicate a positive charge is formed in the transition state and it follows, therefore, that electron donating substituents, such as hydroxyl and methoxyl, having negative σ values, will enhance the reactivity

of aromatic systems according to the Hammett equation: $\log k/k_o = \rho\sigma$. Several studies have been made on the reaction of phenol (17,18) with peroxyacetic acid and the principal products are p-benzoquinone and muconic acid:



The reaction may be envisioned as initial hydroxylation by peroxyacetic acid to give the o- and p-hydroquinones. These are subsequently oxidized to the quinones. The o-quinones further oxidize to the muconic acid by Baeyer-Villiger type reaction.

Studies using methyl aryl ethers (19-21) have shown that they react slower than the free phenols and the methoxyl groups are easily displaced to yield quinones. In general, peroxyacetic acid is not a satisfactory synthetic reagent for phenols or quinones as the products are readily oxidized and yields are generally low.

REACTION WITH LIGNIN-RELATED COMPOUNDS

REACTIONS OF AROMATIC RING OF LIGNIN-RELATED MODEL COMPOUNDS

In a study of the oxidation of various 4-methylphenols and their methyl ethers in glacial acetic acid with 10% PA, Farrand (19) found the main products

to be p-benzoquinones and lactones of muconic acids. The overall reaction scheme is shown in Fig. 2. One of the interesting products is 4-hydroxy-4-methyl-2,5-cyclohexadienone (I) from the PA oxidation of 4-methylphenol (II, R=H). This is very similar to a dienone found by Chambers, et al. (22) and illustrates that PA does act as an hydroxylating reagent under these conditions of oxidation. There were no products reported that showed displacement of the methyl group and this concurs with other studies (22,23). It was also found that the presence of methoxyl or hydroxyl at the C-2 position activated the C-5 position to electrophilic substitution by hydroxyl as evidenced by the formation of the γ-hydroxy lactone III and the p-benzoquinone IV. Also, oxidation of the methyl ethers to the same products as the corresponding phenols shows that PA did effect displacement of methoxyl for hydroxyl. Separate PA oxidation of the muconic acids and the γ-hydroxy lactone showed that these products were relatively unreactive toward further oxidation by PA, while the p-benzoquinone was slowly oxidized to undetermined products. In Farrand's study, the stoichiometry of the oxidation, i.e., the molar ratio of PA to substrate consumed, provided valuable insight into the mechanism of the oxidation processes involved. The relative reactivities of the compounds oxidized in this study are shown in Fig. 3 and these show that free phenols react faster than the ethers and also that a second oxygen-containing substituent significantly increases the rate of oxidation with PA.

As is typical of quantitative product analyses of the reactions of PA with phenolic compounds, the maximum total yields isolated in Farrand's study were low. The highest maximum product yields isolated were approximately 71% for the rather straightforward oxidations of 4-methylpyrocatechol (V) and 4-methyl-o-benzoquinone (VI). The oxidation of the remaining compounds used in his study yielded greater numbers of products and lower yields, ranging from 56.6% for p-cresol (II) to 38.5% for 4-methylveratrole (VII). The low product analyses were

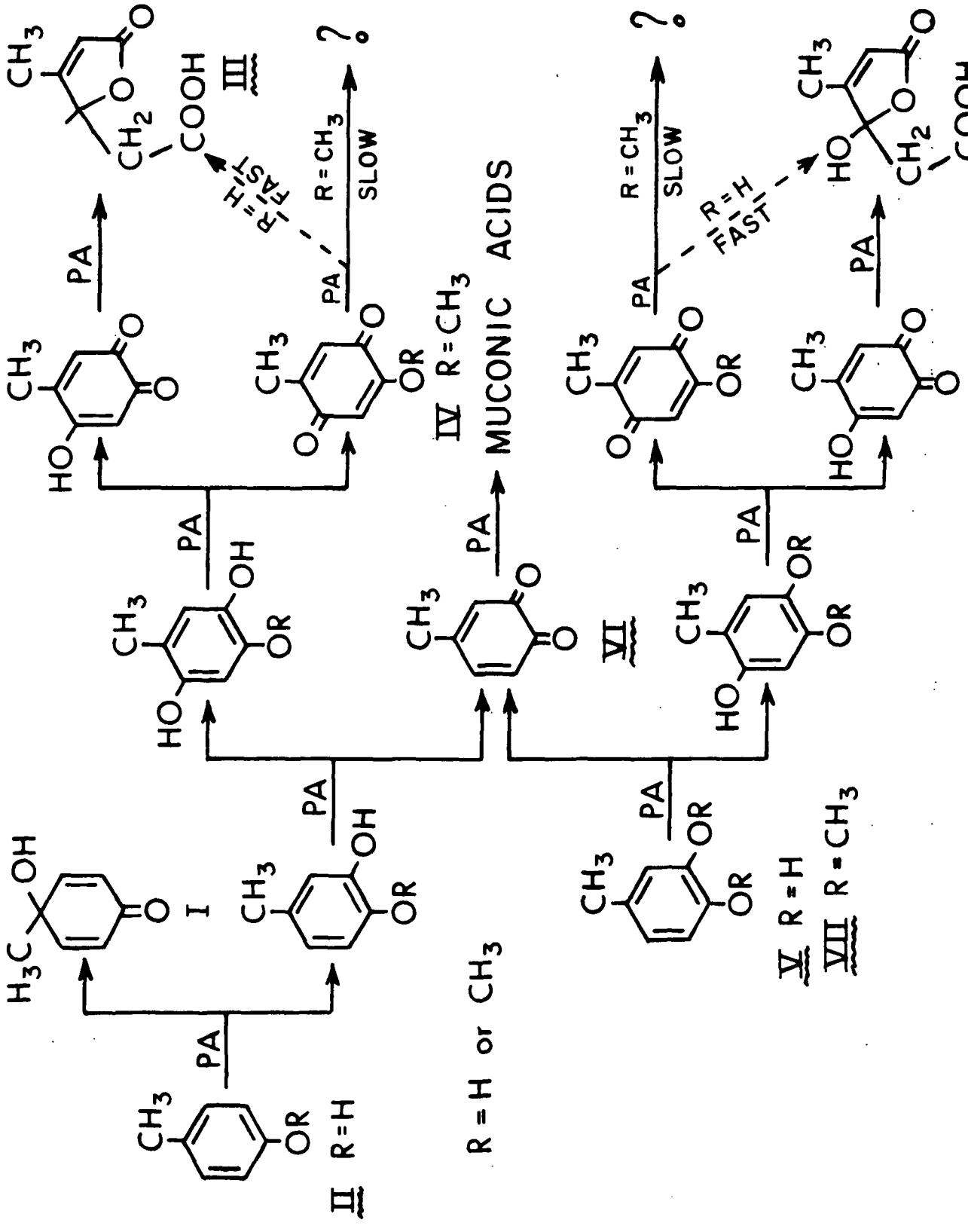


Figure 2. Peroxyacetic Acid Oxidation of 4-Methylphenols and Their Methyl Ethers (19)

interpreted to be the result of incomplete recovery of acidic products, a large number of minor products not quantitated, dimerization of quinone products and intermolecular esterification.

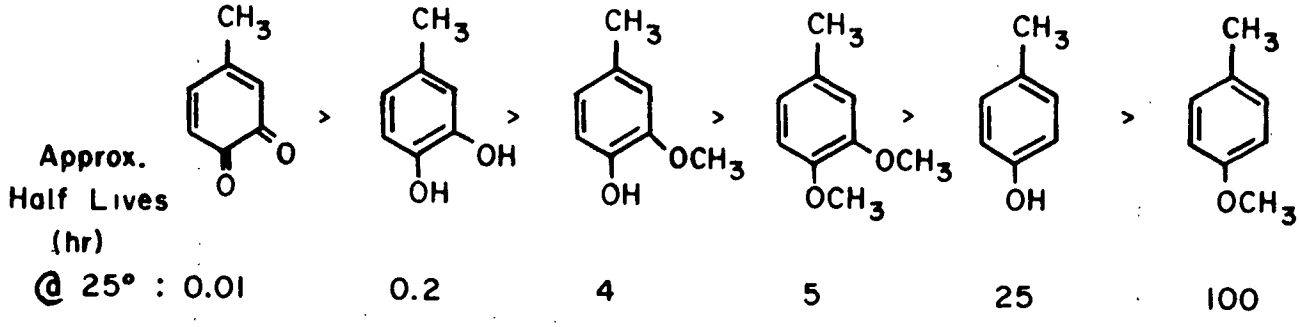


Figure 3. Relative Reactivities of Lignin-Related Model Compounds with Peroxyacetic Acid (19)

REACTIONS OF SIDE CHAIN OF LIGNIN-RELATED MONOMERIC MODEL COMPOUNDS

In Farrand's study (19) the reactions of the aromatic ring of guaiacyl and veratryl type systems were elucidated and this was achieved in part by effectively blocking the 4-position with a methyl group. Several papers have been published (24-27) on the PA oxidation of other lignin-related model compounds containing hydroxy groups in the side chain. The results of two similar studies of model compounds having only an α-(benzylic)hydroxy group are shown in Fig. 4. Hatakeyama, et al. (24) studied the PA oxidation of 3,4-dimethoxybenzyl alcohol (veratryl alcohol, VIII) and 4-hydroxy-3-methoxybenzyl alcohol (vanillyl alcohol, IX, R=H) and found the products connected by the solid lines as shown in Fig. 4. This work shows that the α-hydroxymethyl group is oxidized to a formyl group by PA and subsequently oxidized to a carboxyl in the final product, 4-hydroxy-3-methoxybenzoic acid (vanillic acid, X). Vanillic acid was subsequently oxidized to muconic acids XIa and XIb, and oxalic and maleic acids. Veratryl alcohol reacted via demethylation to give vanillyl alcohol or was oxidized on the side chain to veratraldhyde XII. In a later article, Ishikawa, et al. (25) studied the PA oxidation of α-methyl vanillyl alcohol (IX, R=CH_3), vanillyl alcohol,

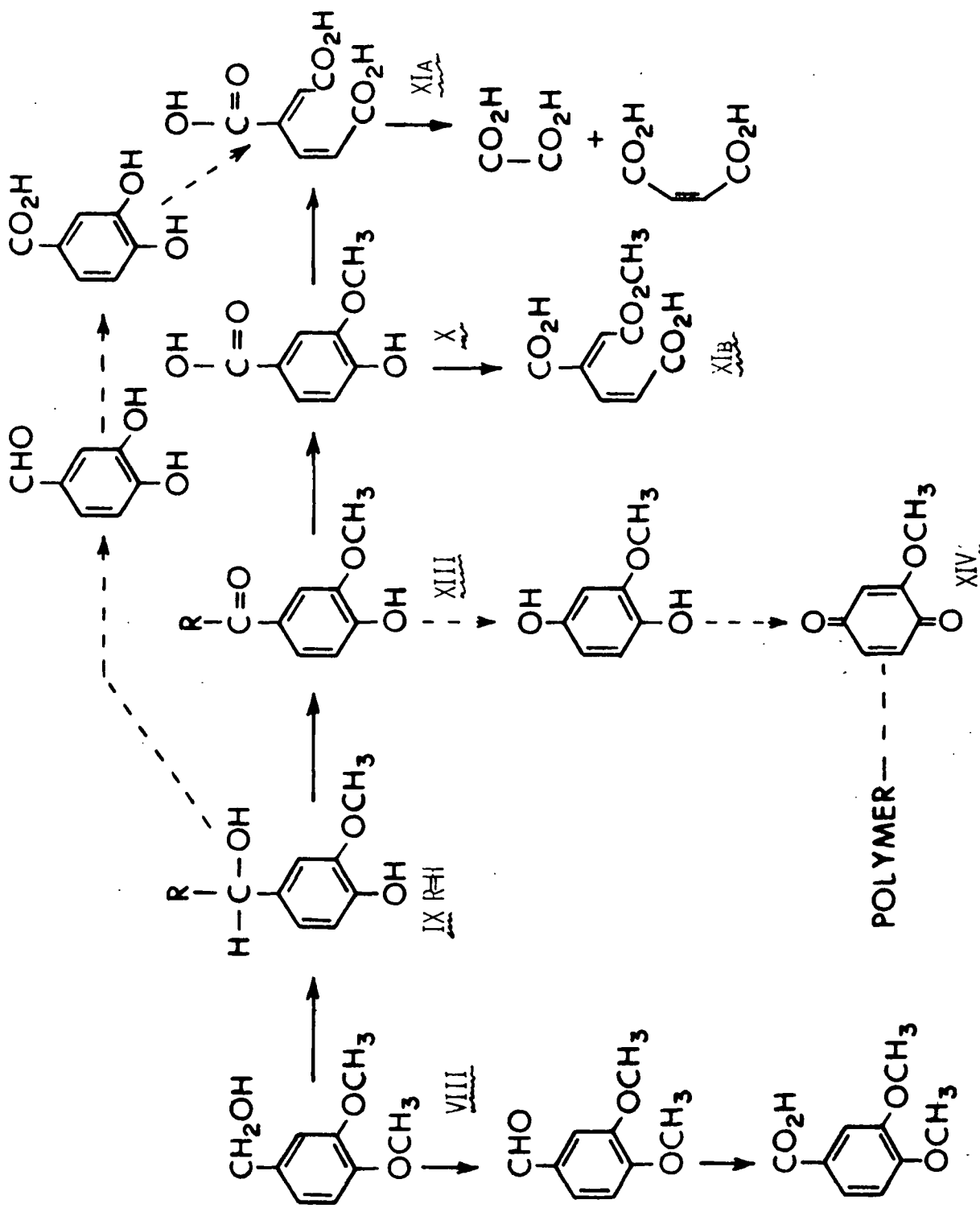


Figure 4. Peroxyacetic Acid Oxidation of Substituted Vanillyl Alcohols (24,25)

vanillin (XIII, R=H), acetovanillone (XIII, R=CH_3) and vanillic acid. In addition to the routes and products reported by Hatakeyama, et al., Ishikawa also reported those indicated by the dashed lines in Fig. 4. These additional products show that the Baeyer-Villiger oxidation of the carbonyl compounds XIII can also lead to the phenolic esters and eventually to the p-quinone XIV. The p-quinone was proposed to lead to polymeric products. Hatakeyama, et al. had reported a substantial portion of their ether extractable products were polymeric but had not proposed any theories concerning the nature or origin of these polymeric products.

Oki and coworkers also reported on the PA oxidation of 1-(4-hydroxy-3-methoxyphenyl)propene (isoeugenol, XV (26)), and 1-(4-hydroxy-3-methoxyphenyl)-propanetriol (guaiacyl glycerol, XVI (27)), and their results are summarized in Fig. 5. Considering first the isoeugenol, the initial reaction is the formation of the epoxide XVII which then leads to the acetate XVIII and the diol XIX by solvolysis. The diol is oxidized to the ketols XX and XXI which are in equilibrium under acidic conditions, the α-keto form being the thermodynamically more stable product (28). The oxidation then proceeds via a Baeyer-Villiger oxidation to vanillin (XXII), 2 methoxyhydroquinone (XXIII) or vanillic acid (X). In the oxidation of guaiacylglycerol (XVI), the proposed initial attack involved a radical process of extraction of a hydrogen atom at the β-carbon atom and subsequent loss of a hydroxyl radical at the α-position to form 2-hydroxyconiferyl alcohol (XXIV), although there was no evidence provided for this mechanism. The alcohol XXIV then undergoes substantial rearrangement to the more stable ketol XX via XXI and the oxidation is then similar to the case of the isoeugenol intermediate oxidation products. In addition, there are side reactions to form 1-(4-hydroxy-3-methoxyphenyl)propan-1-2-diol and 1-(4-hydroxy-3-methoxyphenyl)propan-1,3-diol. These two products were only found in very low yields and were not

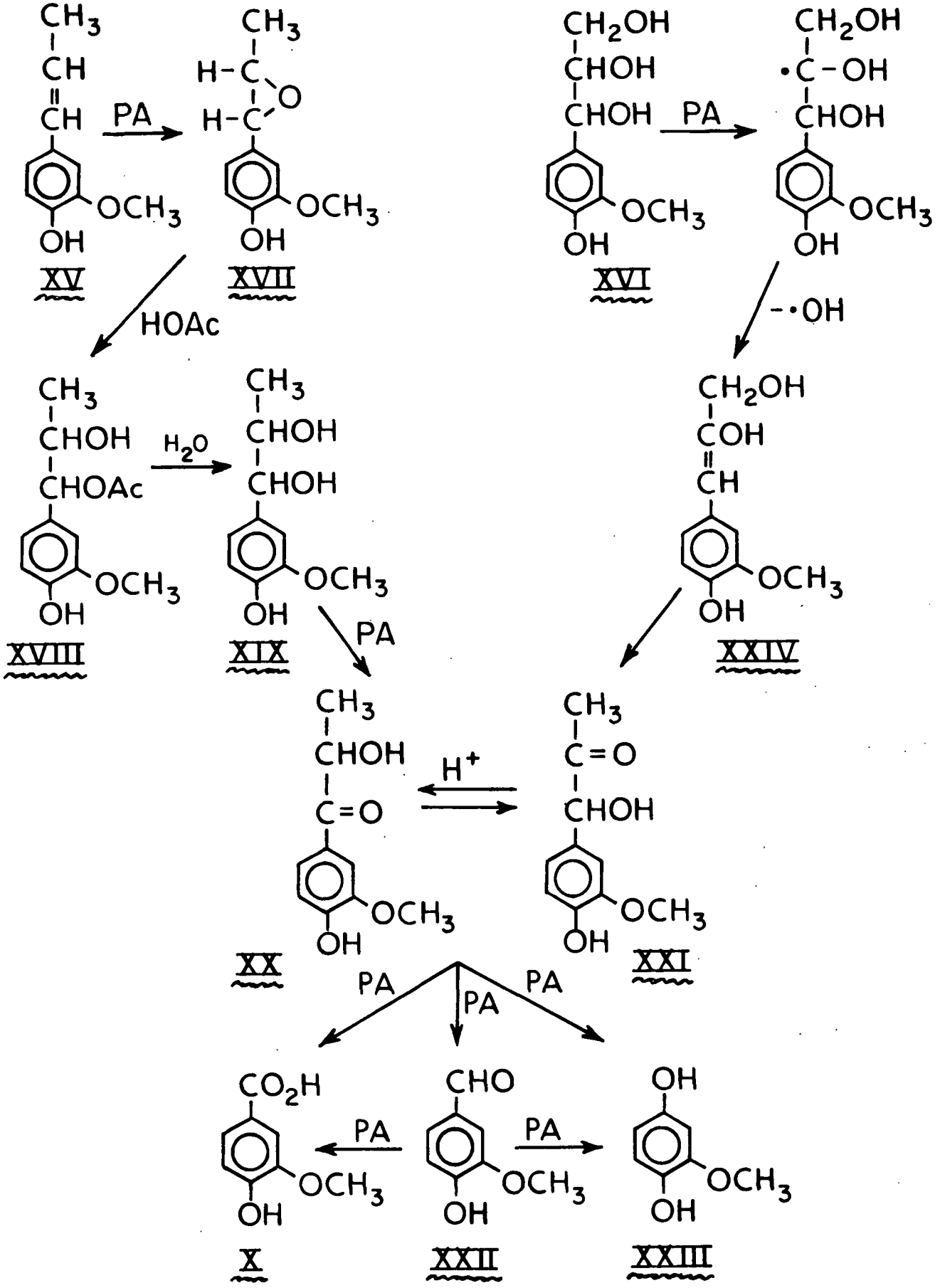


Figure 5. Peroxyacetic Acid Oxidation of Phenylpropyl Type Lignin Related Model Compounds (26,27)

detectable upon treatment of guaiacyl glycerol with similar acetic acid solutions not containing PA.

REACTIONS OF DIMERIC TYPE LIGNIN-RELATED MODEL COMPOUNDS

Several papers have been published on the peroxyacetic acid oxidation of dimerlike lignin related model compounds containing a β-aryl ether linkage (29-31), the most common linkage in lignin (32). Oki, et al. (29) studied the oxidation of 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanol (veratrylglycol-β-guaiacyl ether, VBE, XXV), 1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-ethanol (guaiacylglycol-β-guaiacyl ether, GGE, XXVI), and 2-(2-methoxyphenoxy)-4'-hydroxy-3'-methoxyacetophenone (2-guaiacoxyacetoguaiacone, GAG, XXVII). Based on oxidation products identified, they proposed the reaction scheme shown in Fig. 6. They propose demethylation as a principal mode of reaction; VGE reacts with PA to form GGE and the catechol derivative XXVIII. Also shown in this sequence is oxidation of benzylic hydroxyl group to a carbonyl. Subsequent Baeyer-Villiger oxidations of these keto products give rise to (2-methoxyphenoxy)-acetic acid (XXIX), several substituted benzoic acids and 2-methoxy-p-benzoquinone, XIV. In a subsequent paper (30) on the PA oxidation of 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)propan-1,3 diol (veratrylglycerol-β-guaiacyl ether, VGG, XXX), and 1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)propan-1,3-diol (guaiacyl-glycerol-β-guaiacyl ether, GGG, XXXI), the same workers reported the reaction scheme shown in Fig. 7. They propose that VGG is demethylated to GGG and this reacts according to a major and minor reaction pathway. The major path is cleavage of the β-ether bond to give guaiacol and unspecified guaiacyl propane products. The guaiacol is subsequently oxidized to catechol and muconic acids and the guaiacylpropane products yield vanillic acid. The minor reaction is loss of the γ-hydroxymethyl group to give formaldehyde and GGE XXVI. This reacted similar to results in the previous paper to give the same oxidation products.

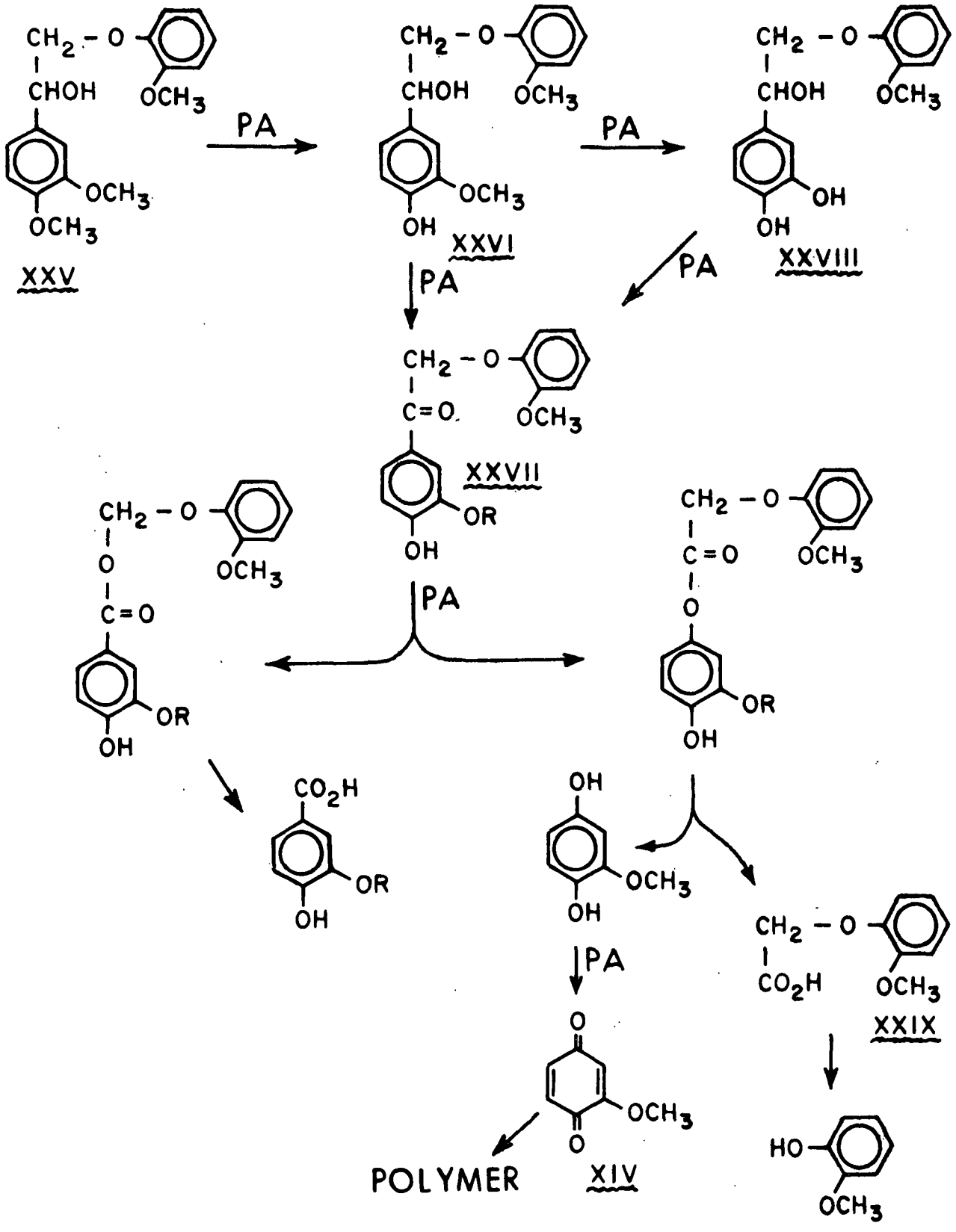


Figure 6. Peroxyacetic Acid Oxidation of Arylglycol-β-aryl Ether Type Lignin Related Model Compounds (29)

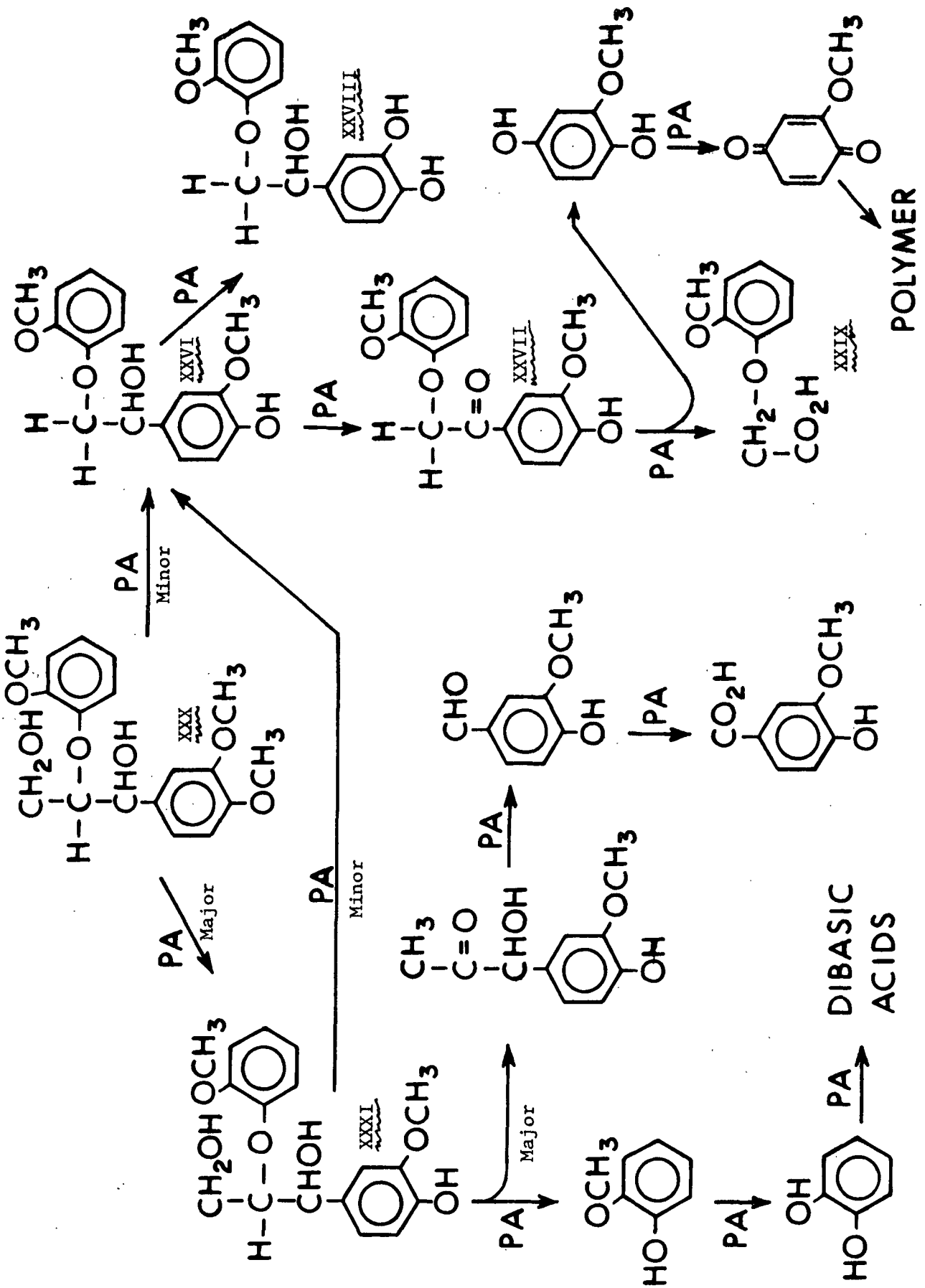


Figure 7. Peroxyacetic Acid Oxidation of Arylglycerol-β-aryl Ether Type Lignin-Related Model Compounds (30)

They found that the minor reactions were affected by the reaction media used, 50% aqueous acetic acid, 50% aqueous ethanol (pH 2.7 and 5.2) and dioxane, giving lower yields of the (2-methoxyphenoxy)acetic acid (XXIX) when the oxidation was run in dioxane.

As would be expected, the total product yields were low. The major products isolated were guaiacol and vanillic acid which accounted for maximum yields of 28% and 12%, respectively. The remaining products were all found in less than 10% yields. Quantitative analyses were performed by measuring UV absorbance of material eluted from a paper chromatogram.

Sakai, et al. (31) studied the PA oxidation of several β-ether model compounds in dioxane and their results are shown in Fig. 8. They found the aldehydes (XXXII, R=H, CH_3) which were formed via electrophilic displacement of the side chain. The aldehydes were subsequently oxidized to (2-methoxyphenoxy)-carboxylic acids XXXIII and the hemiacetal acetates XXXIV via the proposed intermediary hemiacetal formates XXXV by a Baeyer-Villiger oxidation. A minor product that was not confirmed due to low yields was 1-(4-hydroxy-3-methoxyphenyl)propan-1,2-diol.

Guaiacol was the major product isolated in 15% yield. The yield of products resulting from side-chain displacement were significant, amounting to 14.6%. Of this percentage, 8.4% was for XXXIV, 5.2% for XXXII and 1% for XXXIII.

REACTIONS OF PEROXYACETIC ACID WITH WOOD AND ISOLATED LIGNINS

Many studies have been made on the oxidation of wood and isolated lignins with PA. In general, these studies show an increase in carbonyl content with decrease in methoxyl content as could be expected from model compound studies. Sakai and Kondo (33) studied the reactivities of hardwood and softwood dioxane

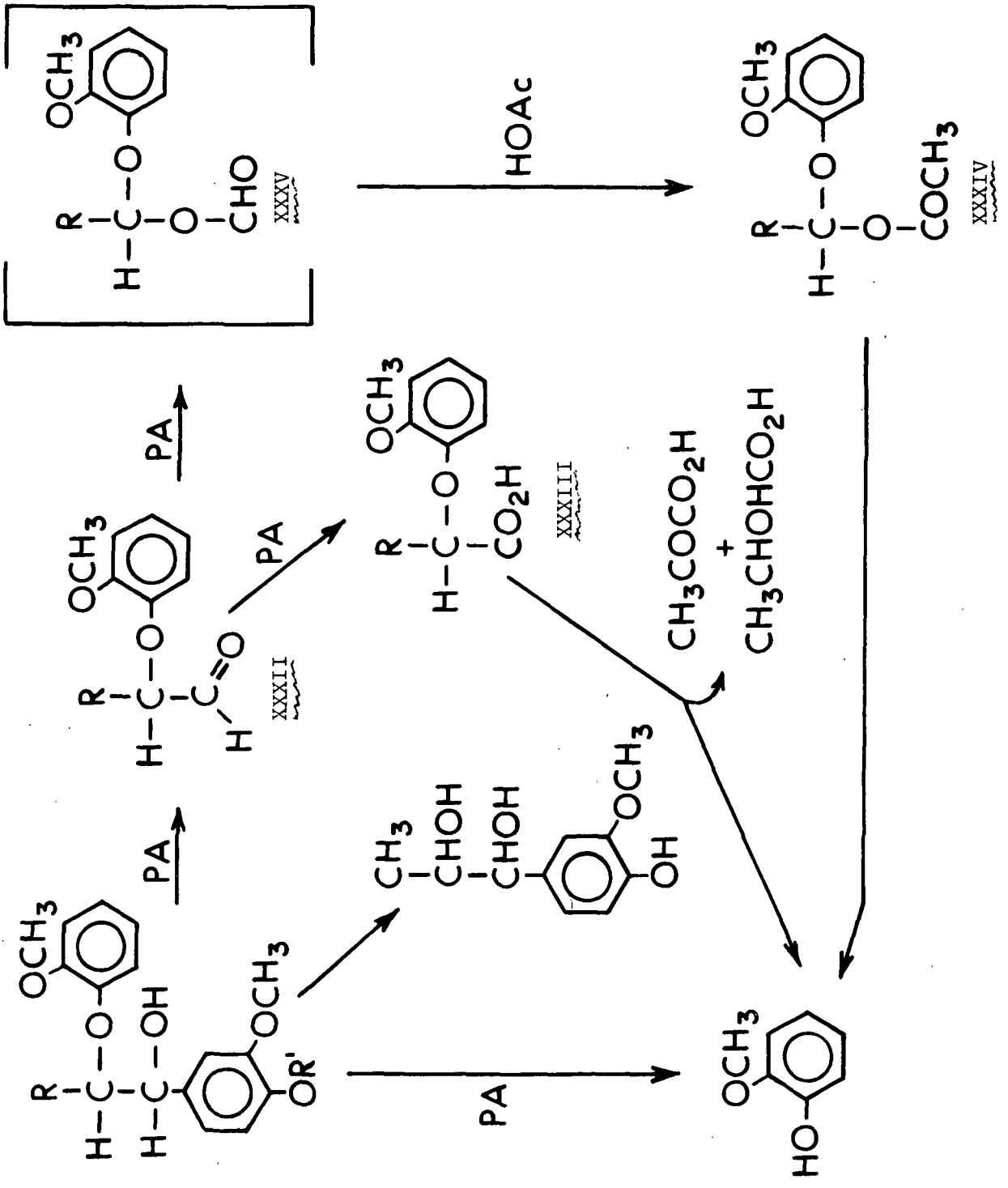


Figure 8. Peroxyacetic Acid Oxidation of β-Aryl Ether Type Lignin-Related Model Compounds (31)

lignins. Yields of vanillin and syringaldehyde by alkaline nitrobenzene oxidation of the PA-oxidized lignins were interpreted to show that syringyl nuclei react 2.5 times more rapidly than guaiacyl nuclei.

In a subsequent paper on the PA degradation of milled wood lignins (34), the same authors reported that β-aryl ether structures were degraded more rapidly than phenylcoumaron type structures. From this data they suggest that degradation of β-aryl ether structures in wood contribute to the solubilization of lignin during peroxyacetic acid oxidation.

Fleck (35) studied the PA oxidation of loblolly pine by pyrolysis of the reacted wood wafers. Analysis of the wafers by pyrolysis-gas chromatography-mass spectrometry (PGCMS) at various yield levels was correlated to results obtained from PGCMS of various model compounds. This technique showed that there was greater oxidation of the phenylpropyl side chain than the aromatic nuclei during the first 1% loss of the wood. Subsequent PA oxidation from 99% to 77% yield was a combination of reaction at the side chain and aromatic ring cleavage with the latter predominating.

PRESENT STUDY

After reviewing the literature, it is evident that there are inconsistencies regarding the reactions of PA with lignin-related β-aryl ether model compounds. These inconsistencies lead to the three specific objectives of this study.

The first deals with the finding of Oki, et al. (30) on the PA oxidation of veratryl type model compounds. Their reaction schemes all show removal of at least one methoxyl group prior to other oxidation reactions. Based on the work of Farrand (19) the veratryl products if formed should be less reactive than the guaiacyl or catechol products found and it should be possible to determine their

presence by presently available techniques. It is not apparent that such demethoxylation should be necessary for the occurrence of the other oxidation reactions that were indicated by the products isolated. The absence of veratryl type PA oxidation products in these studies is suggestive that a peeling type of reaction proceeding from guaiacylglycerol-β-aryl ether-type structures is operative in the PA oxidation of lignin.

A second objective concerns the type of carbon-oxygen bond on the β-carbon atom of the side chain after PA oxidative cleavage of the β-aryl ether bond. Sakai, et al. (31) propose a product that has a hydroxyl group at this position. Oki, et al. (30) have proposed that the arylpropyl product formed in the cleavage of the β-aryl ether bond will have a carbonyl group at the β-carbon atom but have isolated no such compound.

Furthermore, if the β-aryl ether cleavage results in the formation of a substituted phenol (guaiacol in the work of Sakai, et al. (31) and Oki, et al. (30)) and a product having a hydroxyl group on the β-carbon atom, this suggests a hydrolytic or possibly nucleophilic reaction at the β-carbon atom as opposed to an electrophilic aromatic displacement reaction in the aromatic ring.

The third objective concerns the cleavage between the α-carbon atom in the side chain and the aromatic ring. Sakai, et al. (31) propose that this type of cleavage involves electrophilic displacement and Oki, et al. (30) propose this cleavage results from Baeyer-Villiger oxidation of an α-keto oxidation product. Neither sets of workers have been able to find any proof of both types of these reactions and the discrepancy has been dismissed as due to differences in reaction media.

The β-aryl ether model compound to be used in this study is shown in Fig. 9.

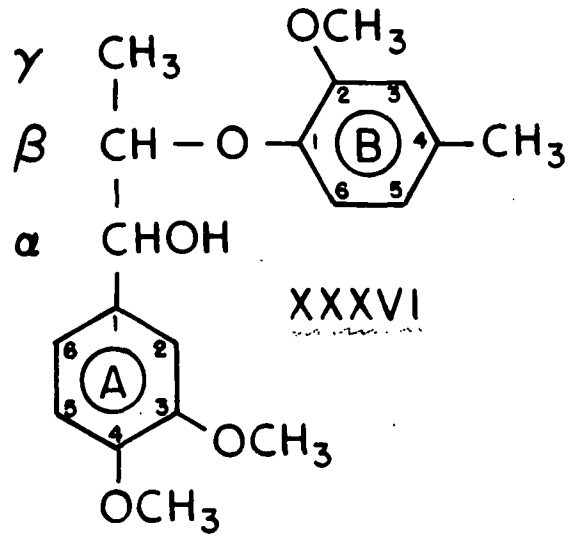


Figure 9. Structure of β-Aryl Ether Model Compound

Using the numbering system shown in Fig. 9, subsequent discussions will refer to the 3,4-dimethoxyphenyl aromatic ring (Ring A) as the veratryl ring and the 2-methoxy-4-methylphenyl aromatic ring (Ring B) will be referred to as the creosol ring. The carbon atoms in the propyl side chain will be referred to as the α-, β-, and γ-carbon atoms with reference to the veratryl ring as is also shown in Fig. 9.

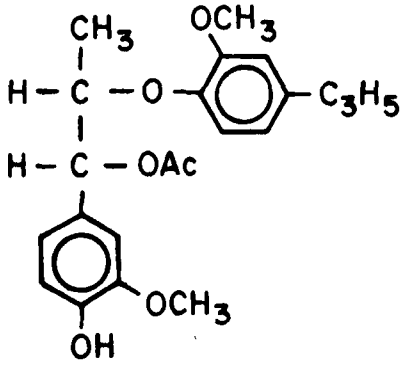
Since Oki, et al. (30) have determined that reactions involving the γ-hydroxymethyl group as found in lignin are minor reactions in this system, the use of a γ-methyl group will not significantly affect the results and will help to center the reactions to those of interest. The 4-position on Ring A, the veratryl ring, is etherified with a methyl group to determine if prior demethoxylation is necessary for PA cleavage reactions of the β-aryl ether structure. The methyl group at the 4-position of Ring B, the creosol ring, is used to block reactions at this position and also serve as a label for oxidation products of this ring. Hydroxylation at this position could lead to p-hydroquinones and their oxidation products and thus could confuse β-ether cleavage with side-chain displacement products from the veratryl ring.

RESULTS AND DISCUSSION

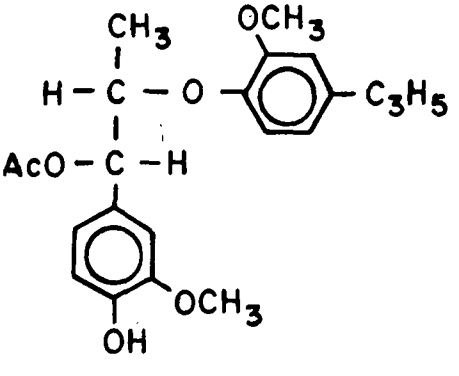
PREPARATION OF COMPOUNDS

The β-ether model compound used in this study, 1-(3,4-dimethoxyphenyl)-2-(2-methoxy-4-methylphenoxy)propanol (XXXVI), was prepared by the synthetic route shown in Fig. 10.

This model compound (XXXVI) always gave a single GLC peak whether analyzed as the alcohol or the trimethylsilyl (TMS) ether. Investigation of the literature gave evidence that the sodium borohydride reduction of the ketone XXXVII would lead to a predominance of the erythro isomer XXXVIa (36,37). The identification of these stereoisomers is most readily obtained by PMR spectra of the acetate derivatives (36). The acetoxy signal of the similar β-aryl ether compounds XXXVIII and XXXIX were found to occur at 2.10 and 2.02 δ, respectively (36).



XXXVIII



XXXIX

Acetylation of β-ether XXXVI and subsequent PMR analysis did indicate that the two isomers were present based on the acetoxy signals at 2.10 and 2.00 δ. The relative amounts of these two isomers, based on the PMR integrals, were estimated to be 94% erythro (2.10 δ) and 6% threo (2.00 δ). This agrees quite well with the literature values that borohydride reduction of similar compounds led to production of 95% of the erythro isomers (36).

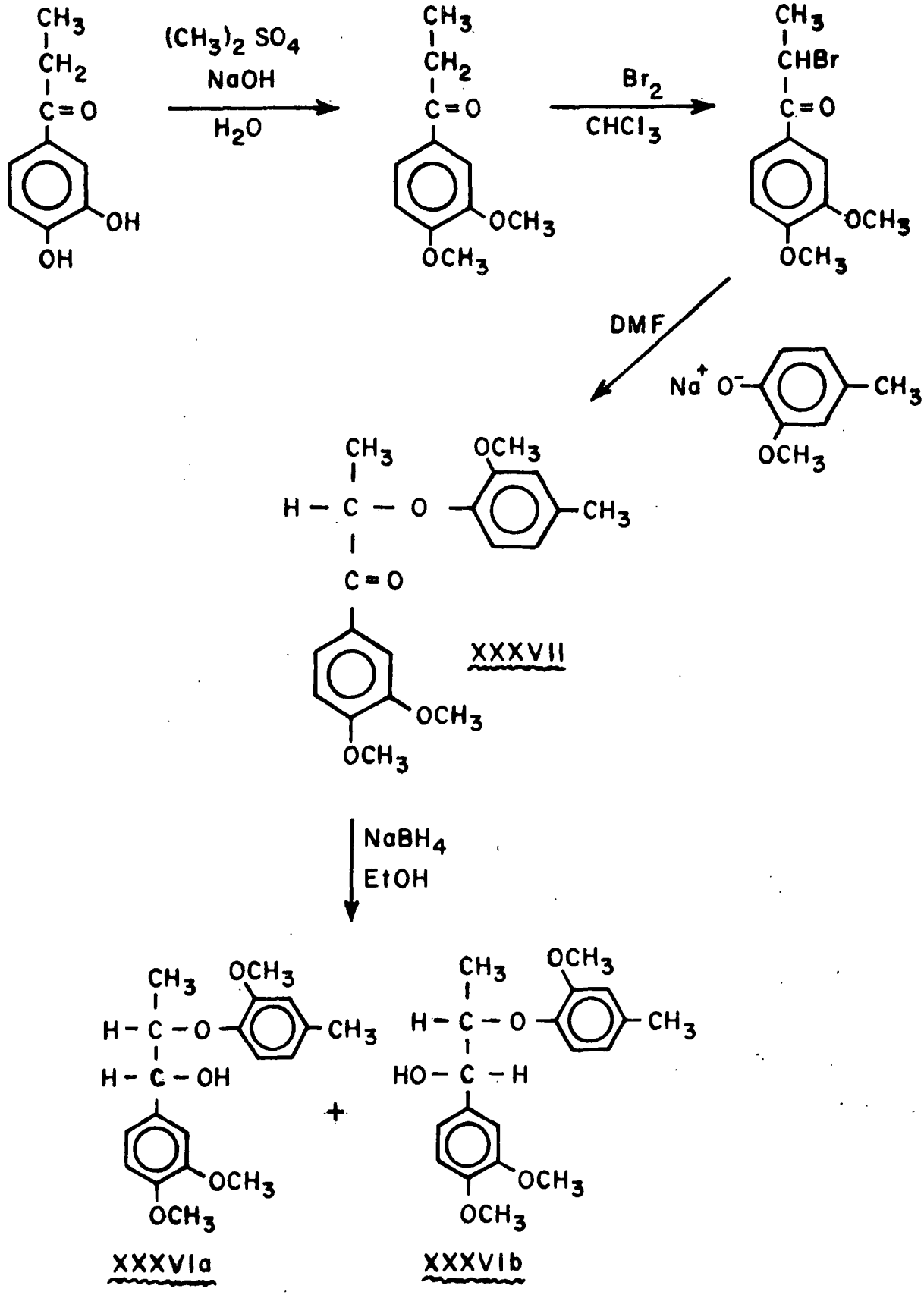


Figure 10. Synthetic Route for Preparation of β-Ether XXXVI

The reactivities of the two major phenylpropyl PA oxidation products of XXXVI were also investigated in this study. These two products, erythro 1-(3,4-dimethoxyphenyl)propan-1,2-diol (diol XLa) and 1-(3,4-dimethoxyphenyl)-1-hydroxy-propan-2-one (ketol XLI) are shown in Fig. 11. Diol XLa was the major PA oxidation product of β-ether XXXVI found in this investigation. The final synthetic reaction that was used in the preparation of a known sample of diol XL was the sodium borohydride reduction of 3',4'-dimethoxy-2-hydroxypropiophenone. Similar to the reduction of ketone XXXVII, the predominant product formed was the erythro isomer (XLa) by comparison with the melting point of the known erythro isomer as reported in the literature (38). Analysis by GLC of the bis-TMS ether showed that there was a minor impurity (∿1%) having slightly greater retention time. The mass spectrum of its TMS derivative was identical to that for XLa and it was concluded the impurity was the threo isomer.

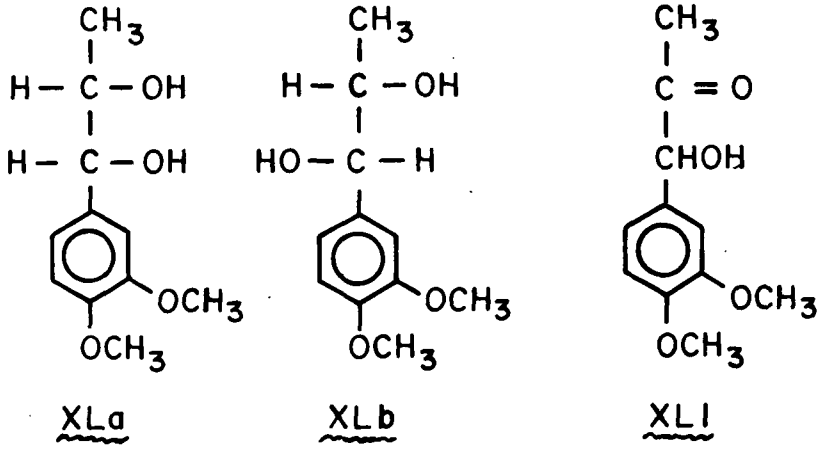


Figure 11. Arylpropyl Type Model Compounds Used in This Study

PEROXYACETIC ACID OXIDATION OF MODEL COMPOUNDS

The oxidations of the model compounds used in this study were run at 25°C in 2.5% peroxyacetic acid using a 5:1 mole ratio of PA to substrate. The hydrogen peroxide concentration was kept low by using freshly generated PA. Aliquots were

withdrawn at appropriate times for analysis of PA, starting material and oxidation products. To prevent further oxidation after sampling, the residual PA was reduced by a minimum (5-10%) excess of sodium sulfite.

REACTIVITY OF MODEL COMPOUNDS IN 2.5% PEROXYACETIC ACID

The oxidations of β-ether XXXVI, diol XL, and ketol XLI by 2.5% PA are shown in Fig. 12. The half-life of β-ether XXXVI is 23.5 hours and is comparable to results reported for a similar compound 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)propan-1,3-diol which was 60% reacted in 24 hours (30). Comparison to the oxidation of diol XL shows that the absence of the creosol ring causes a decrease of about 50% in the reactivity. This suggests that a significant amount of the oxidation of β-ether XXXVI is involved with the oxidation of the creosol ring system. Comparison of the reactivity of diol XL and ketol XLI shows that there is a very significant increase in reactivity upon the inclusion of a carbonyl function in the molecule. This is similar to results of other workers in comparing the reactivity of compounds containing α-hydroxy and α-carbonyl substituents (29,31) and shows that reaction of carbonyls by a Baeyer-Villiger oxidation is appreciably faster than aromatic ring oxidation involving electrophilic aromatic substitution.

In the oxidation of ketol XLI there was a significant amount of 3,4-dimethoxyphenol (XLII in Fig. 13) formed. This product was isolated by column chromatography and subsequently identified by its PMR and mass spectra. A possible reaction pathway for the PA degradation of ketol XLI is shown in Fig. 13. Lundquist and Hedlund (28) have shown that under acidic conditions ketol XLI isomerizes to 3',4'-dimethoxy-2-hydroxypropiophenone (XLIII) and that this ketol is the thermodynamically favored isomer. Since the yield of XLII is not a maximum at zero time, as shown in Fig. 14, the formation of phenol XLII results from the

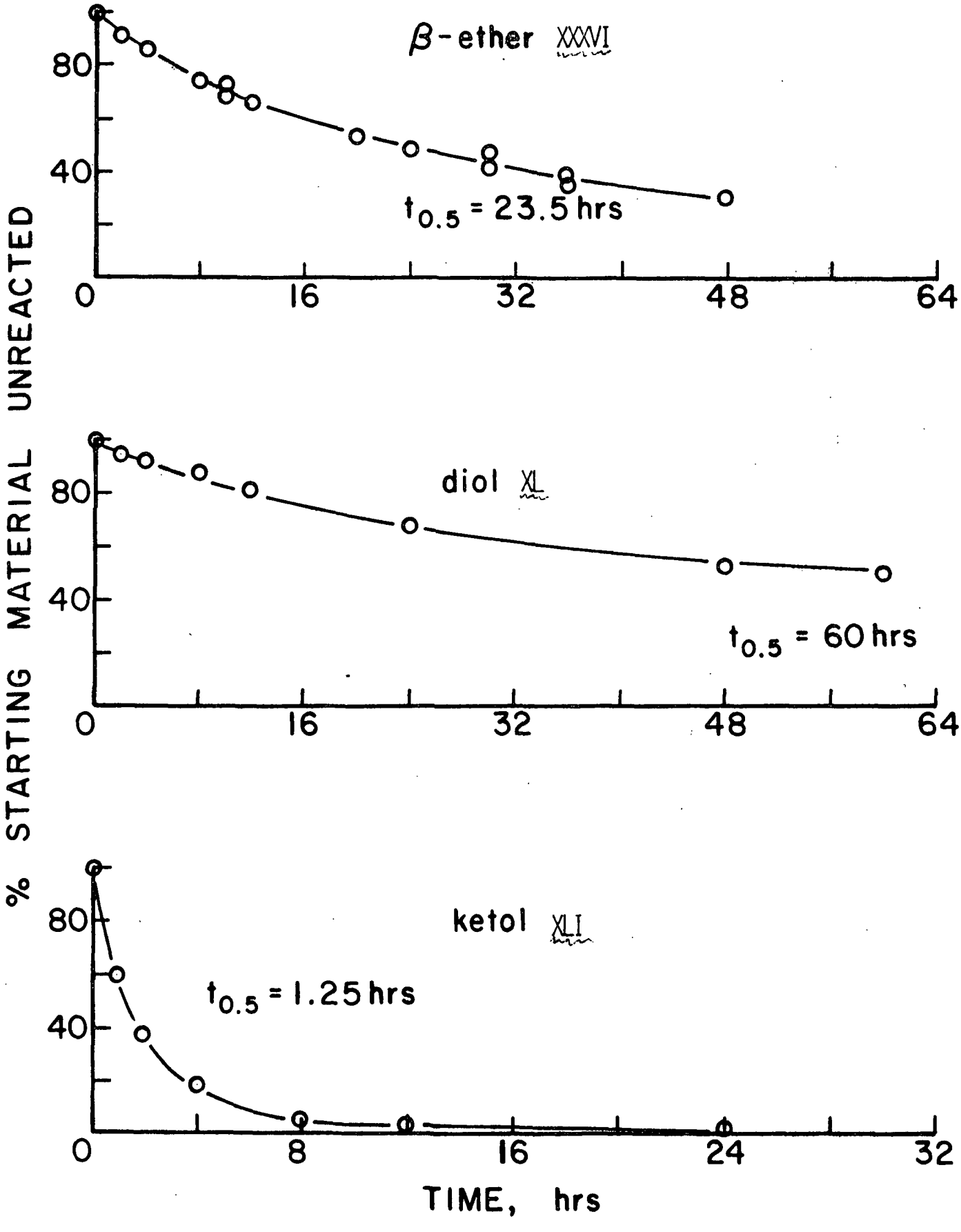


Figure 12. PA Oxidation of Model Compounds

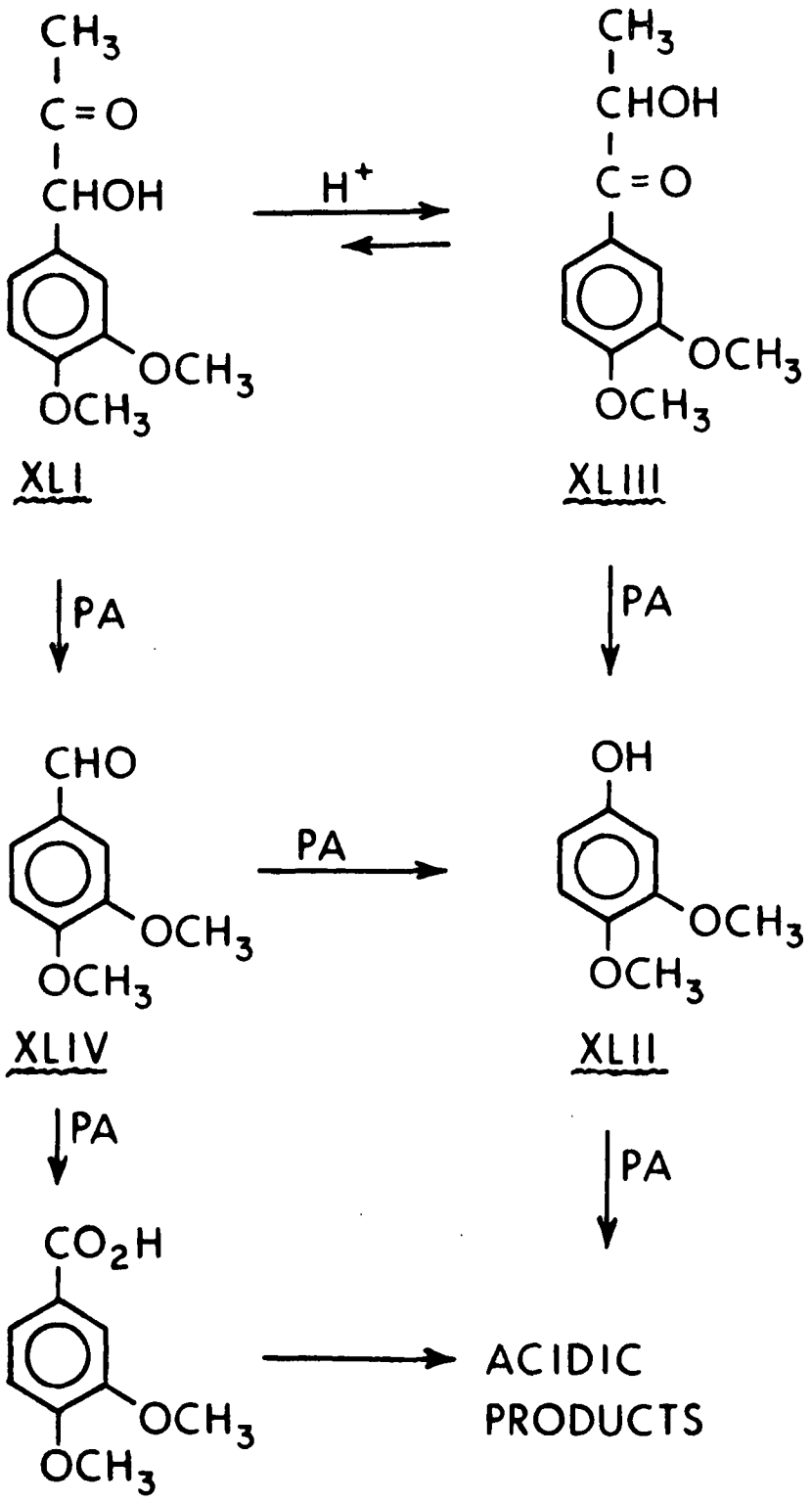


Figure 13. PA Oxidation of Ketol XLI

oxidation of a primary product and not as the result of direct oxidation of ketol XLI.

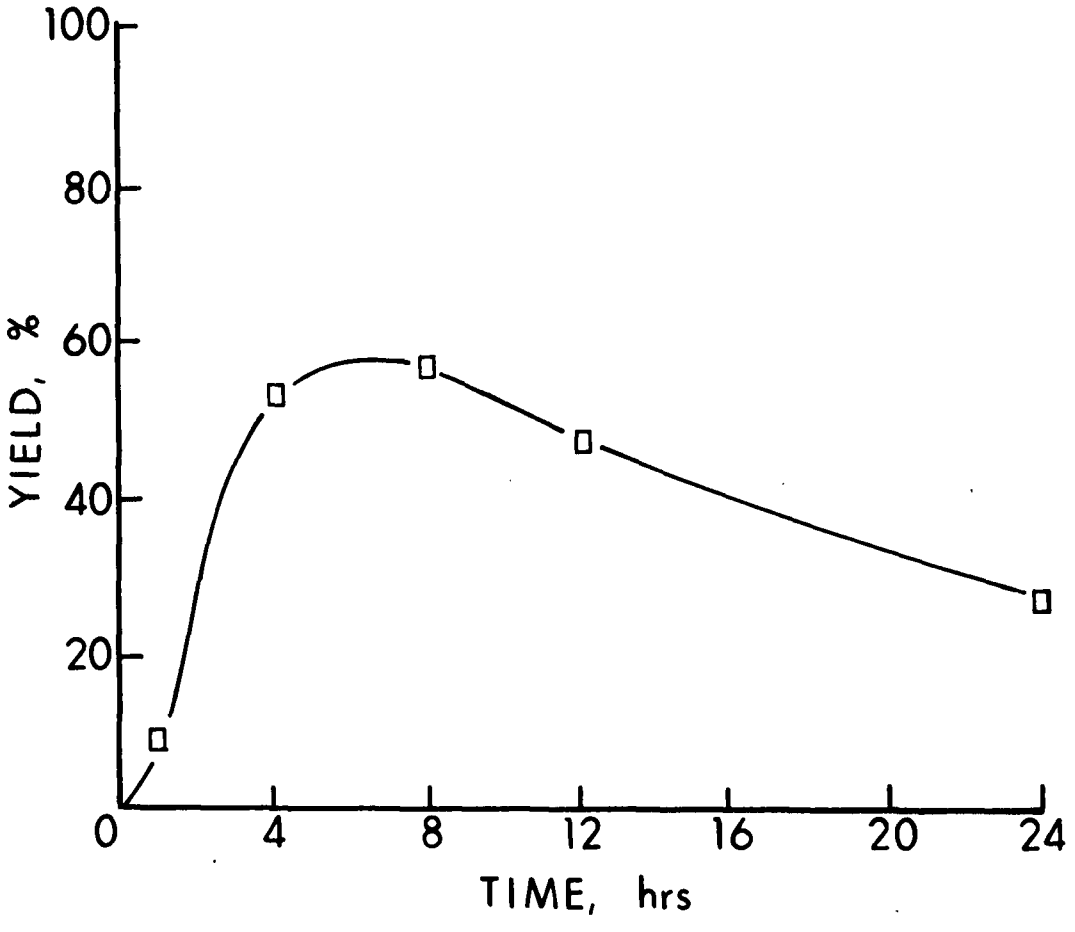


Figure 14. Yield [based on consumed starting material (XLI)] of DMP (XLII) as a Function of Time in PA Oxidation of Ketol XLI

STOICHIOMETRY OF PEROXYACETIC ACID OXIDATIONS OF MODEL COMPOUNDS

The stoichiometry, that is, the ratio of moles of PA consumed to moles of substrate consumed, of these three oxidations is shown in Fig. 15. The extrapolations of the stoichiometry of β-ether XXXVI and ketol XLI to zero time indicate an initial stoichiometry between 1 and 2. Previous work has shown that both Baeyer-Villiger oxidation and aromatic ring oxidation are first order with respect to peroxyacids. This indicates, therefore, that the initial oxidation products are quite reactive and consume additional peroxyacetic acid. In the case of diol

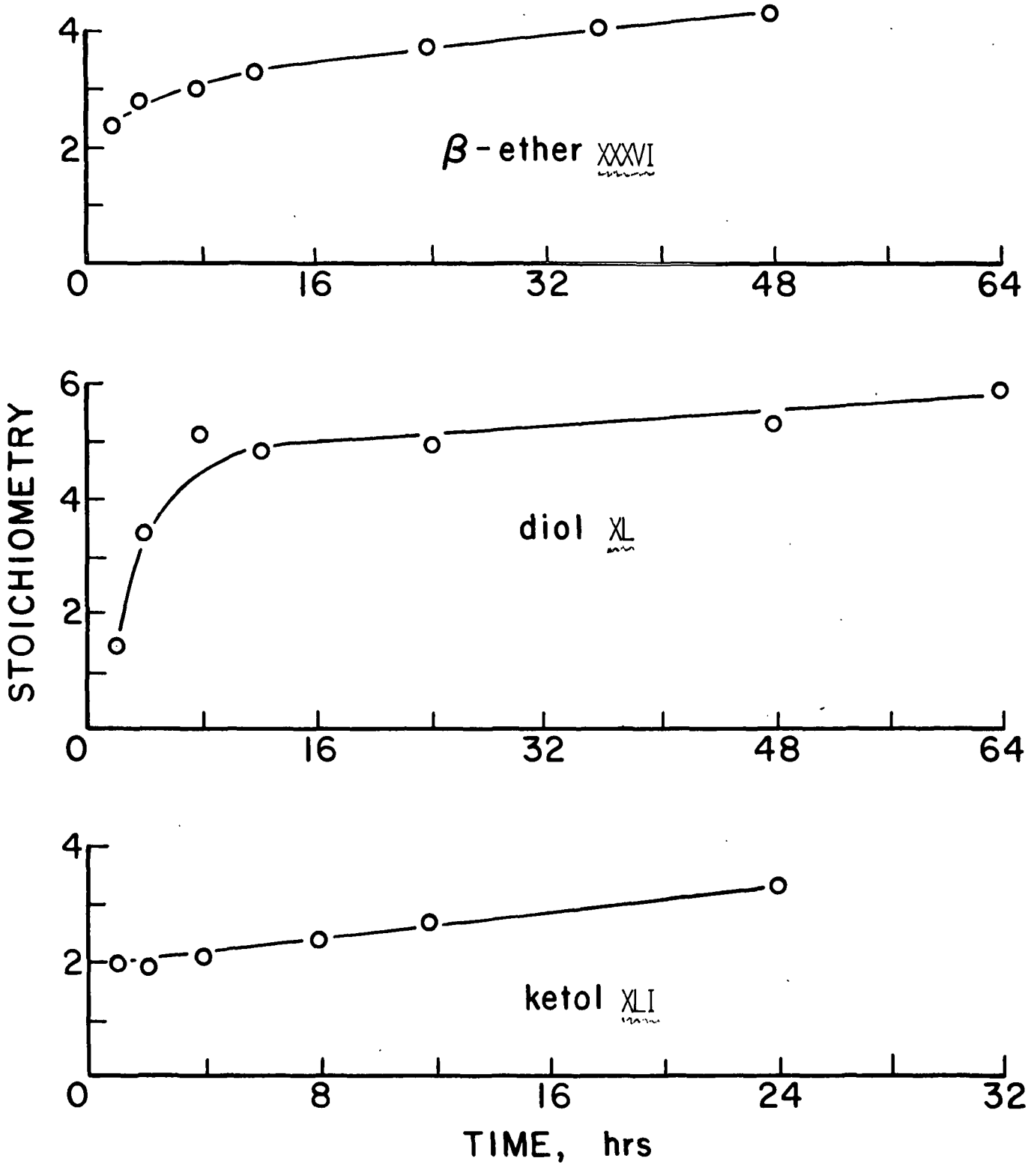


Figure 15. Stoichiometry of Peroxyacetic Acid Oxidations

XL there is a rapid rise in stoichiometry to a nearly constant level of 5.5-6. This indicates that the product or products resulting from initial reactions of the peroxyacetic acid with diol XL are further oxidized quite extensively to presumably acidic products. In the analysis of the PA oxidation of diol XL there were no significant amounts of neutral and phenolic products found as in the cases of ketol XLI and β-ether XXXVI.

PEROXYACETIC ACID OXIDATION PRODUCTS OF β-ARYL ETHER MODEL COMPOUND

Approximately 0.01 mole of β-aryl ether XXXVI was oxidized for 24 hours in 2.5% PA. After reduction of excess PA with sodium sulfite, the products were separated into neutral-phenolic and acidic fractions by an extractive procedure. Following preliminary fractionation by column chromatography, the oxidation products were converted to their TMS derivatives where possible and further fractionated by preparative gas chromatography. In this manner, a large number of oxidation products were isolated in sufficient purity and quantity to allow definitive structural assignments to be made based on proton magnetic resonance and mass spectra of the TMS derivatives of the oxidation products. Known samples were available for a majority of the oxidation products and additional proof of structure was provided by comparison of the GLC retention times and mass spectra of the appropriately derivatized (acetylated or trimethylsilylated) known samples with similar data for the oxidation products. In some cases, alternative or additional techniques such as TLC R_f values, melting point and infrared spectrophotometry were used. The products identified in the PA oxidation of β-ether XXXVI are shown in Fig. 16. The products are divided into six groups based on their structural similarities.

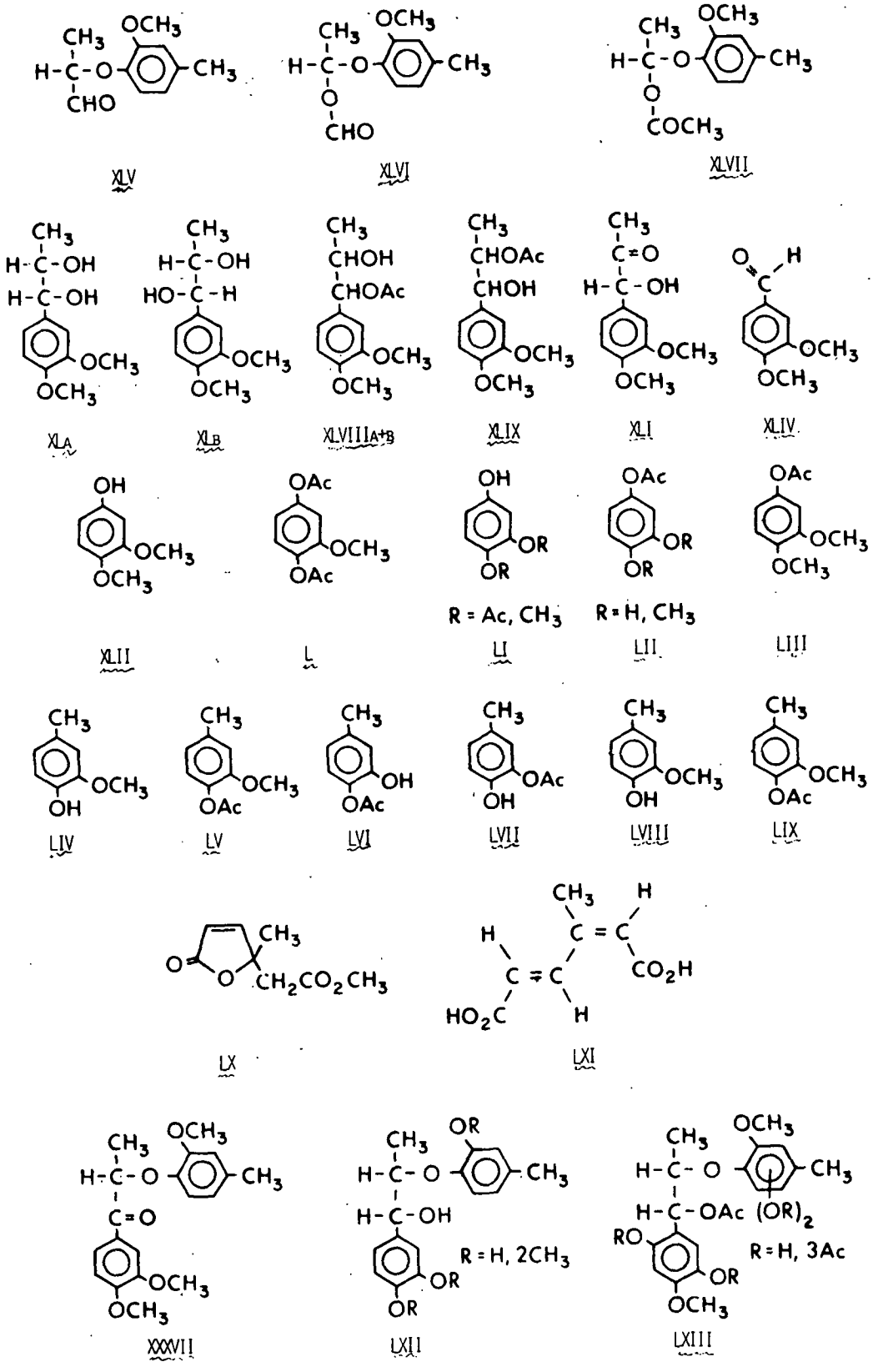


Figure 16. Products from Peroxyacetic Acid Oxidation of β-Aryl Ether Model (XXXVI)

QUANTITATIVE PRODUCT ANALYSIS OF β-ARYL ETHER MODEL COMPOUND

The yields (based on reacted starting material) of the neutral and phenolic products of the PA oxidation of β-ether XXXVI as a function of time are shown in Fig. 17. Figure 18 shows a sample chromatogram of a derivatized oxidation product sample. It was necessary to use additional separation techniques, column and preparative gas chromatography, to obtain sufficient amounts and purity of the minor products for structural determinations. The maximum amount of reacted starting material accounted for (4-hr oxidation sample) was 38%.

The top graph in Fig. 17 shows the yields of diol XL and its related products. The yield of the erythro (XLa) and threo isomers (XLb) of diol XL after 2 hours of reaction was 20.9 and 1.9%, respectively. This gives a ratio of erythro to threo isomer of 91.7% to 8.3% which is very similar to the percentages of the erythro and threo isomers (94 and 6%, respectively) found for β-ether XXXVI as calculated by integration of the PMR spectra of the acetate derivatives. The maximum combined yield of diol XL and its related products is 23.6%. This shows that the oxidation of β-ether XXXVI to diol XL represents a major route for the PA oxidative cleavage of β-ether XXXVI. The decreasing yields of this product with time reflect the oxidation of these diols.

The yields of creosol (LIV) and its derivatives, LV, LVIII and LIX, are shown in the middle graph in Fig. 17. The initial increase in yield with time indicates that creosol is being formed as a secondary product in the oxidation, and therefore it is not possible to make an accurate estimate of the amount of creosol formed from the primary oxidation of β-ether XXXVI.

The yields of XLV and XLVII are plotted together in the bottom graph in Fig. 17. These two products were overlapping peaks in the gas chromatograph as can

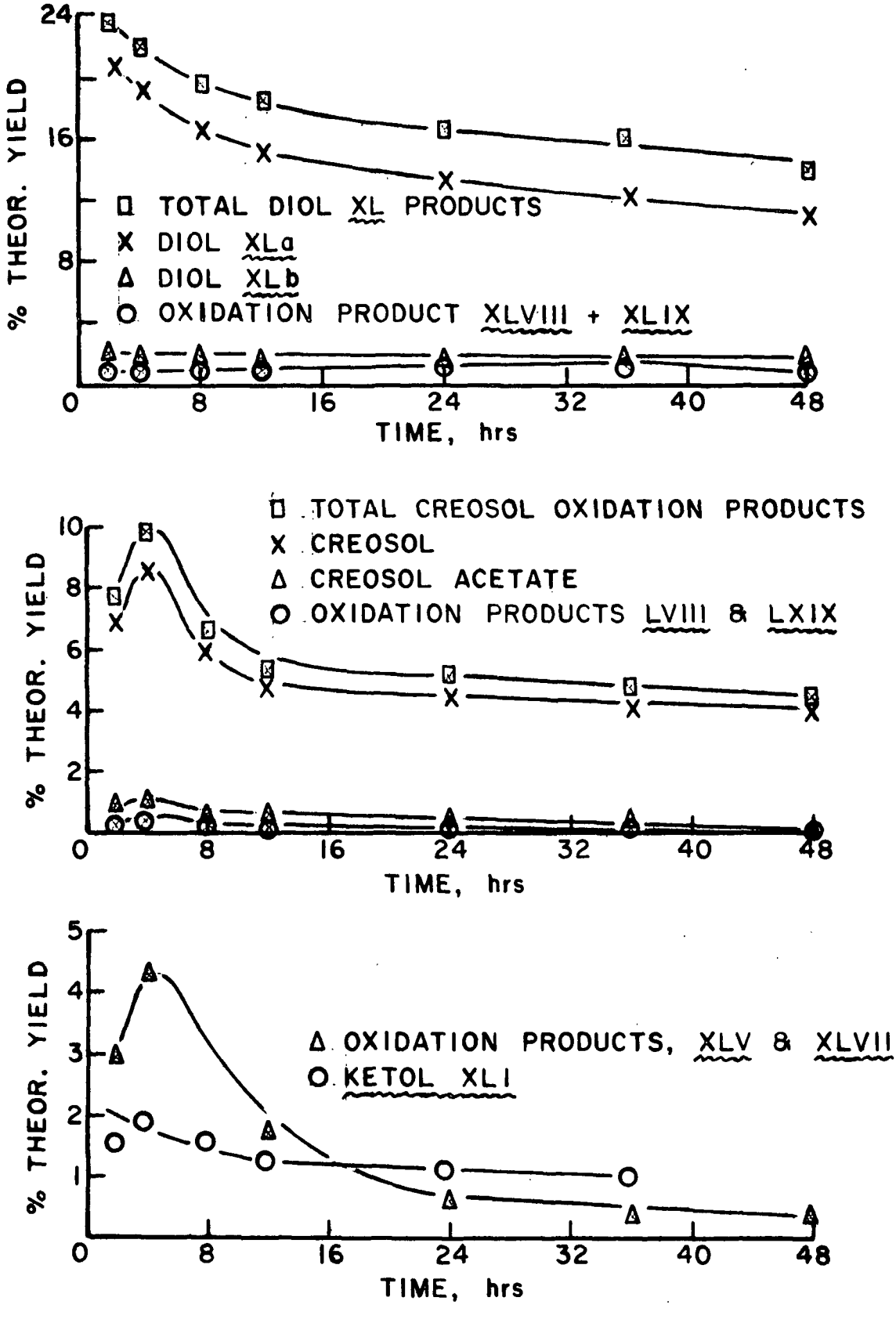


Figure 17. Yield of PA Oxidation Products of β-Ether XXXVI

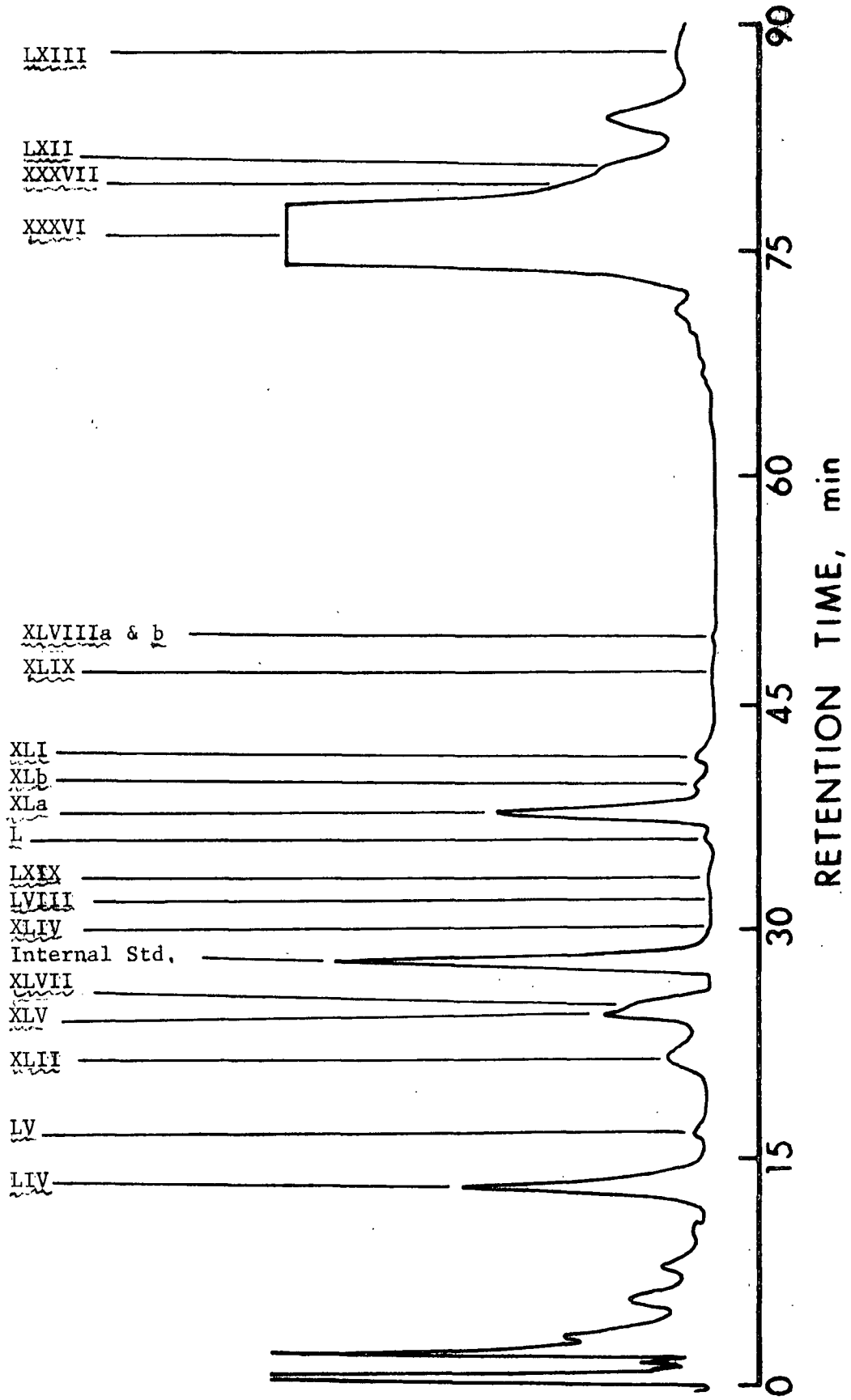


Figure 18. Sample Chromatogram for PA Oxidation Products of β-Ether XXXVI

be seen in Fig. 18. Due to this overlapping and the fact that XLVII is an oxidation of XIV, no attempt was made to quantitate the peaks separately.

The yield of ketol XLI is also shown in the bottom graph in Fig. 17. As might be expected due to its high reactivity, the yield of this product is very low and the actual percentage of β-ether XXXVI leading to this product is likely to be considerably greater than 2% as the maximum yield in Fig. 17 shows.

As can be seen from the sample chromatogram of the neutral and phenolic products in Fig. 18, the dimeric products do not give very well defined peaks. In addition, their retention times were quite variable since these peaks did not elute until the upper temperature limit used in the temperature programmed gas chromatograph had been reached.

PRIMARY OXIDATION REACTIONS OF β-ARYL ETHER MODEL COMPOUND

Based on the qualitative and quantitative results shown in Fig. 16 and 17, an oxidation scheme showing the major primary oxidative pathways for the PA oxidation of β-ether XXXVI is shown in Fig. 19. In this oxidation scheme it is proposed that there are three major routes leading directly to bond cleavage between the two aromatic rings and these are shown by Paths A, B, and C. Path D, involving oxidation of the α-hydroxyl to carbonyl does not result directly in cleavage of the interaryl linkage. However, subsequent PA oxidation of the ketone XXXVII does result in cleavage products that are different than those of Paths A, B, or C. The fifth pathway, Path E, results in ring hydroxylation other than at position 1 of the veratryl or creosol rings. While reactions of this type do not result directly in cleavage between the aromatic rings, they can activate the molecule toward further attack by PA that will cleave the interaryl linkage. With the exception of quinone VI, all of the remaining oxidation products indicated in Fig. 19 were isolated and identified in this study.

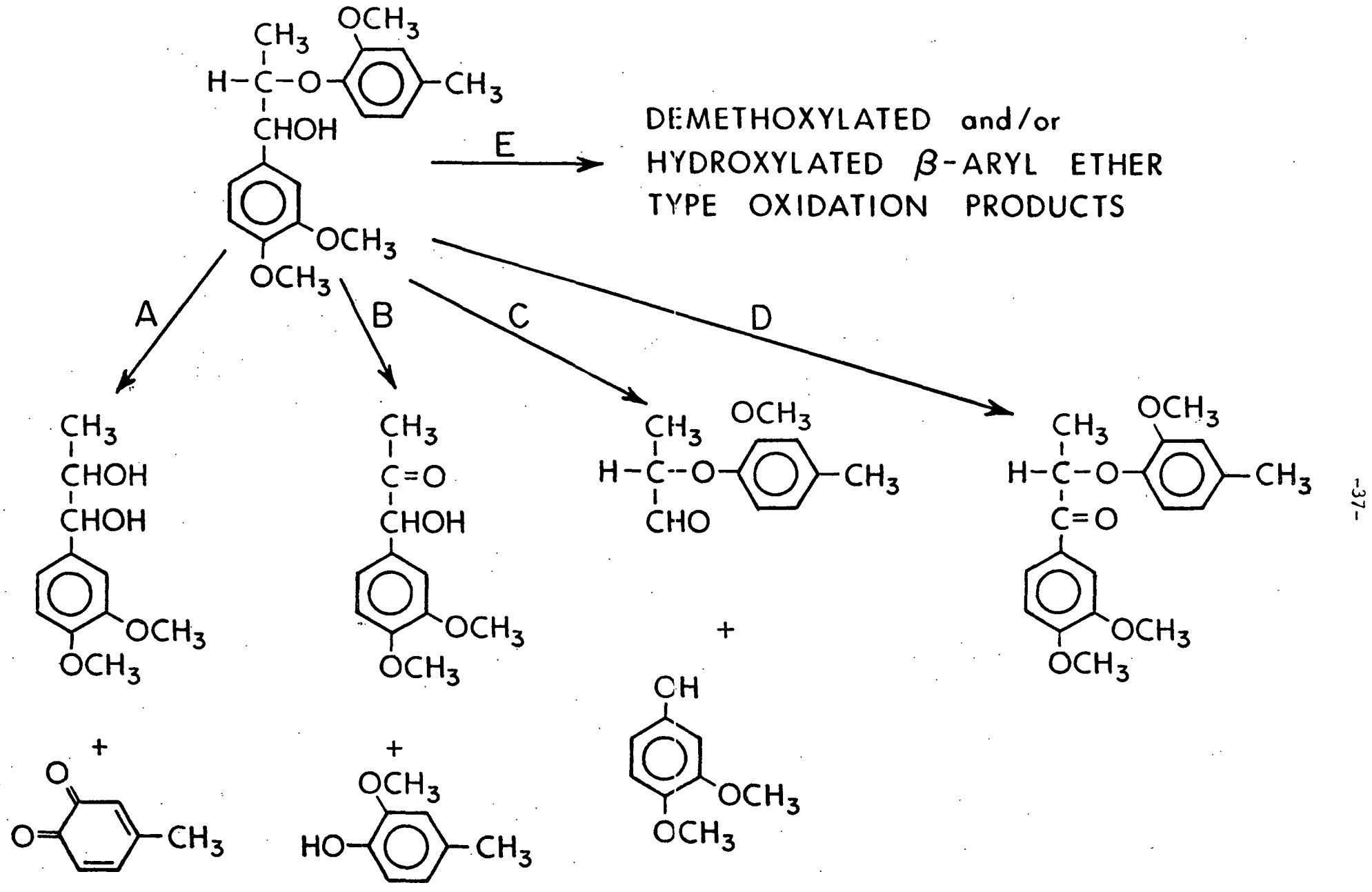


Figure 19. Major Oxidative Pathways in PA Oxidation of β-Ether XXXVI

The reactions A-D can be subdivided into two groups. Paths A and B result in cleavage of the β-aryl ether bond in β-ether XXXVI as a result of electrophilic substitution on the creosol ring. Paths C and D result in cleavage of the propyl ether bridge between the two aromatic rings as the result of cleavage reactions about the α-carbon atom of the β-aryl ether linkage.

β-ARYL ETHER BOND CLEAVAGE, OXIDATION PATH A

There are two possible mechanisms (I and II) for the oxidative formation of diol XL from β-ether XXXVI. Mechanism I, shown in Fig. 20, involves initial attack of PA on the creosol ring at the 2 position of the creosol ring or that of the methoxy substituent. Support for the attack at this position and not the 6 position comes from previous work on the PA oxidation of ortho dimethoxy model compounds (19) where the major products have all resulted from the initial attack of PA at one of the methoxy substituted positions. Farrand's work (19) also indicated a smaller amount of substitution at the 5 position but no mention was made of products resulting from attack at a position equivalent to the 6 position. This initial attack leads to the resonance stabilized carbonium ion LXIV in Fig. 20. It is then proposed that neighboring group assistance from the benzylic hydroxyl leads to cleavage of the ether bond with formation of the protonated epoxide LXV and the methyl hemiketal. Subsequent hydrolysis gives 4-methyl-o-benzoquinone (VI) and diol XL. During the course of the reaction the erythro product remains the major product as expected from neighboring group participation. If the mechanism involved a free, secondary carbonium ion, molecular models suggest that the threo isomer would be the major product. Similar participation of hydroxyl groups has been proposed by March (38).

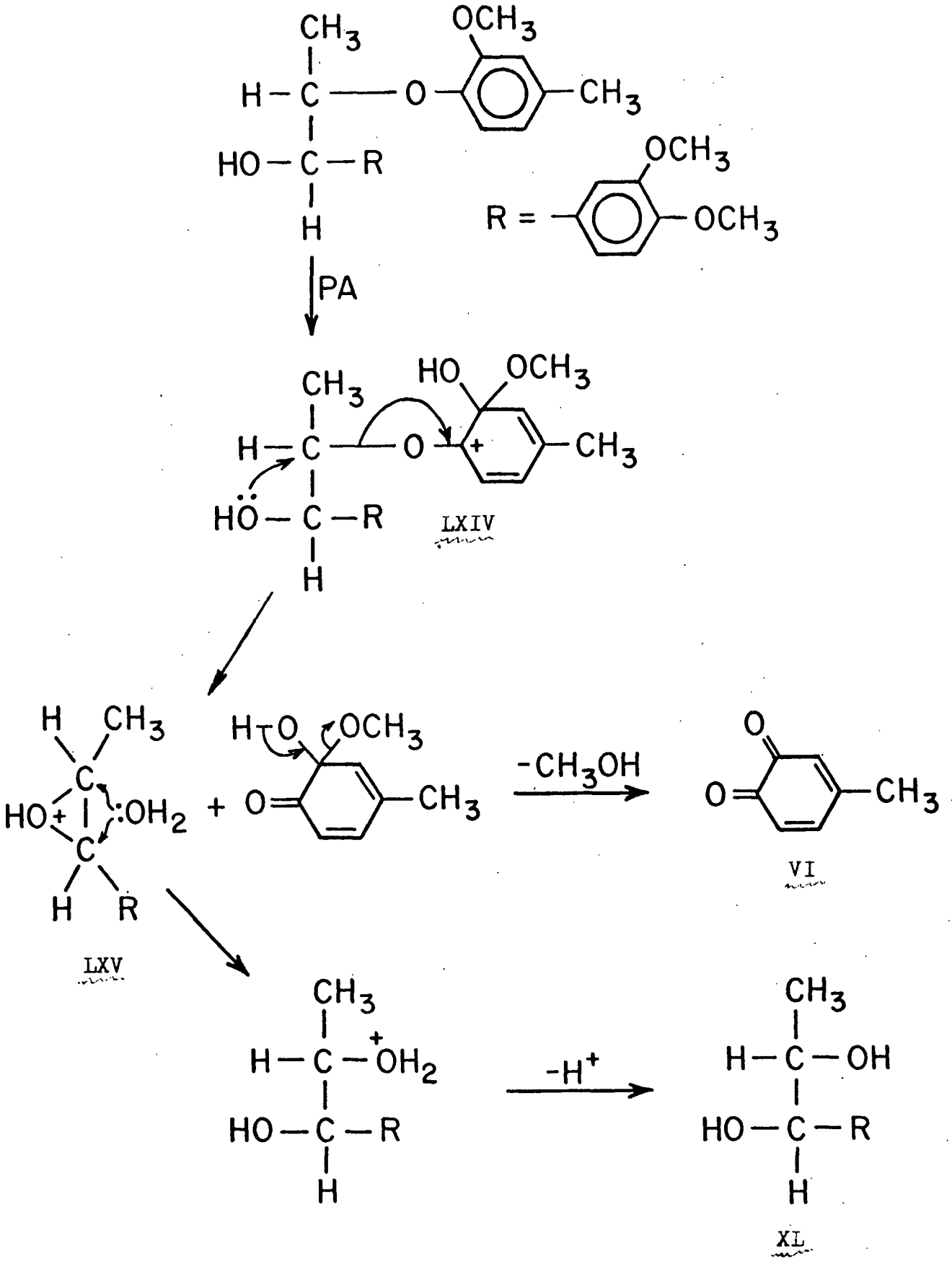
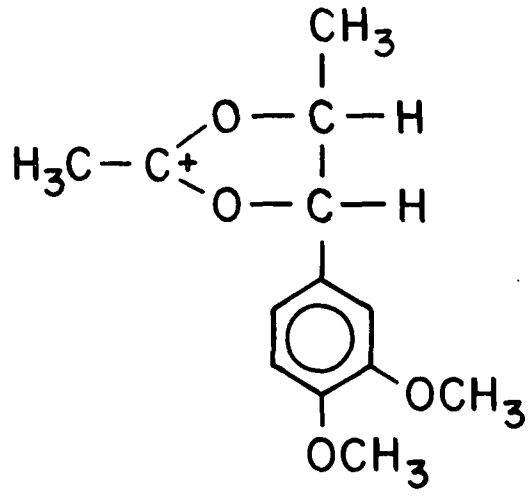


Figure 20. Possible Mechanism (I) for Formation of Diol XL in PA Oxidation of β-Ether XXXVI

This mechanism becomes even more favorable if there is acetylation of the benzylic hydroxyl group. In this case the positive charge can be developed on the more stable acetoxonium ion LXVI as shown below.



LXVI

The second mechanism for this cleavage reaction, shown in Fig. 21, involves initial attack at the 1 position of the creosol ring. Interaction of the carbonium LXVII formed with the solvent leads to the ortho-dihemiketal LXVIII. Subsequent hydrolysis of LXVIII leads to diol XL and ortho-quinone VI. This mechanism also leads to retention of the stereochemistry as found experimentally.

As previously discussed, the formation of diol XL in the PA oxidation of β-ether XXXVI appears to be a primary reaction and can account for greater than 20% of the oxidized XXXVI. In view of these facts and the substitution of the creosol ring, it would not be expected that such a major product would result solely from initial attack at the 2 position of the creosol ring. It is expected that the 1 position would be favored for initial electrophilic attack due to the activation of this position by both the 2-methoxy and the 4-methyl substituents. On the other hand, the isolation of the monoacetyl derivatives of diol XL, XLVIII and XLIX, is suggestive that the acetoxonium ion LXVI or the epoxide LXV may participate in cleavage of the β-aryl ether bond of XXXVI by PA. The results

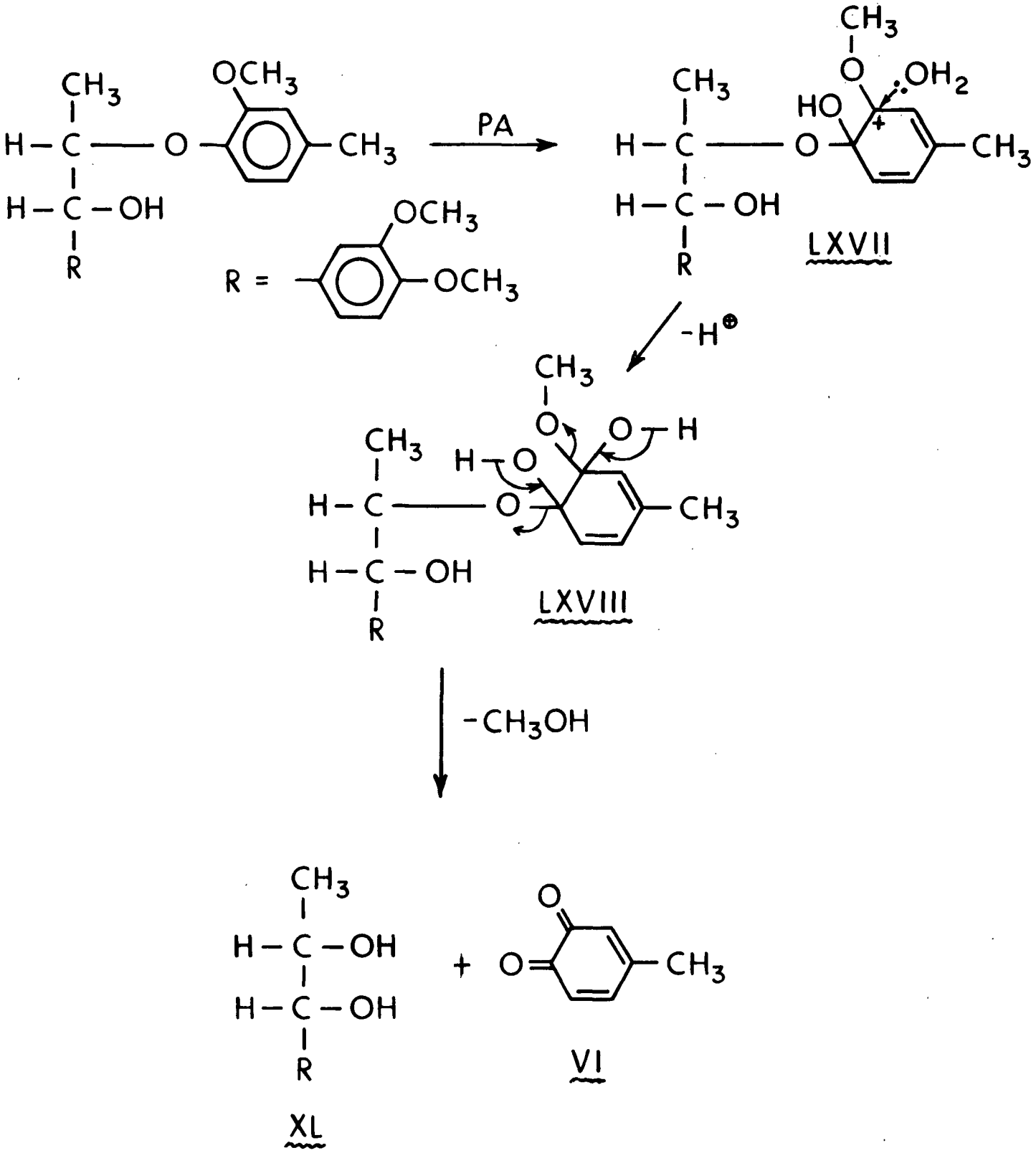


Figure 21. Possible Mechanism (II) for Formation of Diol XL in the PA Oxidation of β-Ether XXXVI

found in this study do not allow for differentiation between the relative importance of these two mechanisms.

β-ARYL ETHER BOND CLEAVAGE, OXIDATION PATH B

The proposed mechanism for the formation of ketol XLI and creosol (LIV) in the PA oxidation of β-ether XXXVI is shown in Fig. 22. The initial attack of PA again involves hydroxylation of the creosol ring and in this case the position of attack is the 1 position, the point of attachment of the arylpropyl ether bond. Loss of the proton on the β-carbon atom of the side chain results in the formation of creosol and ketol XLI.

The occurrence of products mechanistically related to the creosol found in this study have been found in all of the previous PA oxidation studies of β-aryl ether type model compounds (29-31). The isolation and identification of 1-(3,4-dimethoxyphenyl)-1-hydroxypropan-2-one (ketol XLI) in this study is the first reported finding of the remaining fragment of the β-aryl ether cleavage leading to creosol or its analogs. The independent study of the PA oxidation of ketol XLI, which showed a much greater reactivity with PA than the starting material, indicates that the yield isolated for this product is considerably less than that actually produced in the PA oxidation of the β-ether XXXVI.

REACTIVITY OF β-ARYL ETHER MODEL COMPOUND IN AQUEOUS ACETIC ACID

The finding of creosol and diol XL as major products might suggest that these products are formed simultaneously by a hydrolytic as opposed to oxidative cleavage of the β-aryl ether bond of XXXVI (39). Hydrolysis of β-ether XXXVI was attempted in glacial acetic acid and 95% aqueous acetic acid for extended times at 25°C, the temperature used for the PA oxidations. These results are shown in Table II and they show that the starting material was completely recovered in both media.

In addition, the gas chromatograms did not show any extraneous peaks such as found in the oxidation samples. From these data it is concluded that these products formed do not result from hydrolysis but rather from the PA oxidation of β-ether XXXVI.

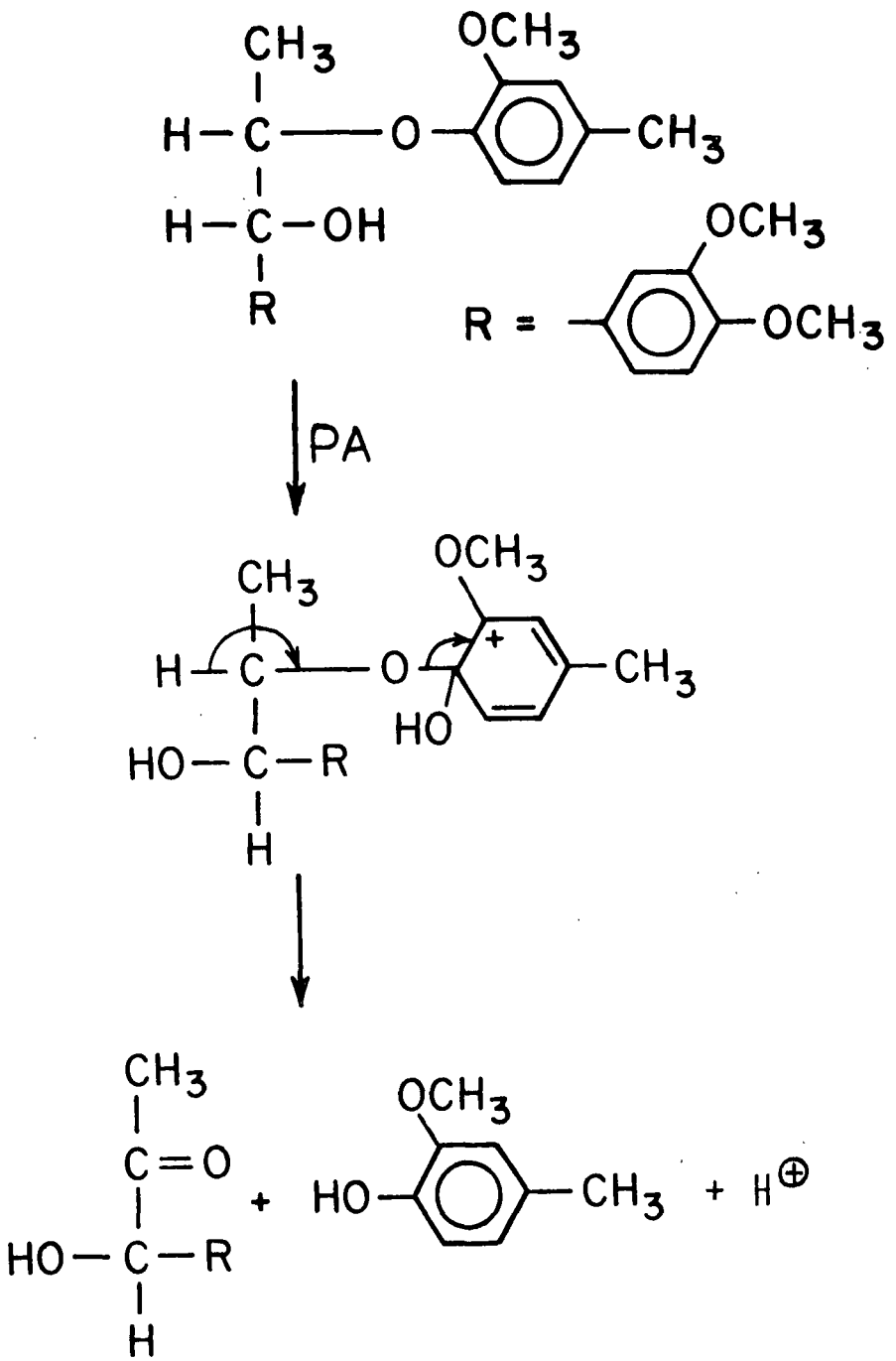


Figure 22. Possible Mechanism for Formation of Ketol LXI in the PA Oxidation of β-Ether XXXVI

TABLE II

THE ATTEMPTED HYDROLYSIS OF β-ETHER XXXVI

[XXXVI] (mg/g)	Time (hr)	% Recovery
Solvent — Glacial Acetic Acid		
23.45	0	--
24.35	72	103.8
Solvent — 95% Aqueous Acetic Acid		
19.27	0	--
19.98	24	103.6
19.50	48	101.1

SIDE-CHAIN DISPLACEMENT, OXIDATION PATH C

A mechanism for the formation of oxidation product XLV is shown in Fig. 23. This mechanism, involving electrophilic displacement of the side chain, is reasonable based on the known ability of peroxyacids to undergo these types of reactions with aromatic systems. Sarkanen and Dence (40) have proposed a similar mechanism for the side-chain displacement in reactions of substituted benzyl alcohols with chlorine. Their work also showed the importance of the benzyl hydroxyl in the mechanism as side-chain displacement was substantially decreased by etherification of the benzylic hydroxyl group.

The isolation and characterization of 2-(2-methoxy-4-methylphenoxy)propionaldehyde XLV and the hemiacetal esters, 1-(2-methoxy-4-methylphenoxy)ethyl formate XLVI and 1-(2-methoxy-4-methylphenoxy)ethyl acetate XLVII also confirms the previous findings of Sakai, et al. (31) that electrophilic side-chain displacement does occur in the PA oxidation of lignin-related model compounds containing a benzylic hydroxyl group. The reactions leading to formation of the hemiacetal esters are shown in Fig. 24. Baeyer-Villiger oxidation of the aldehyde XLV can

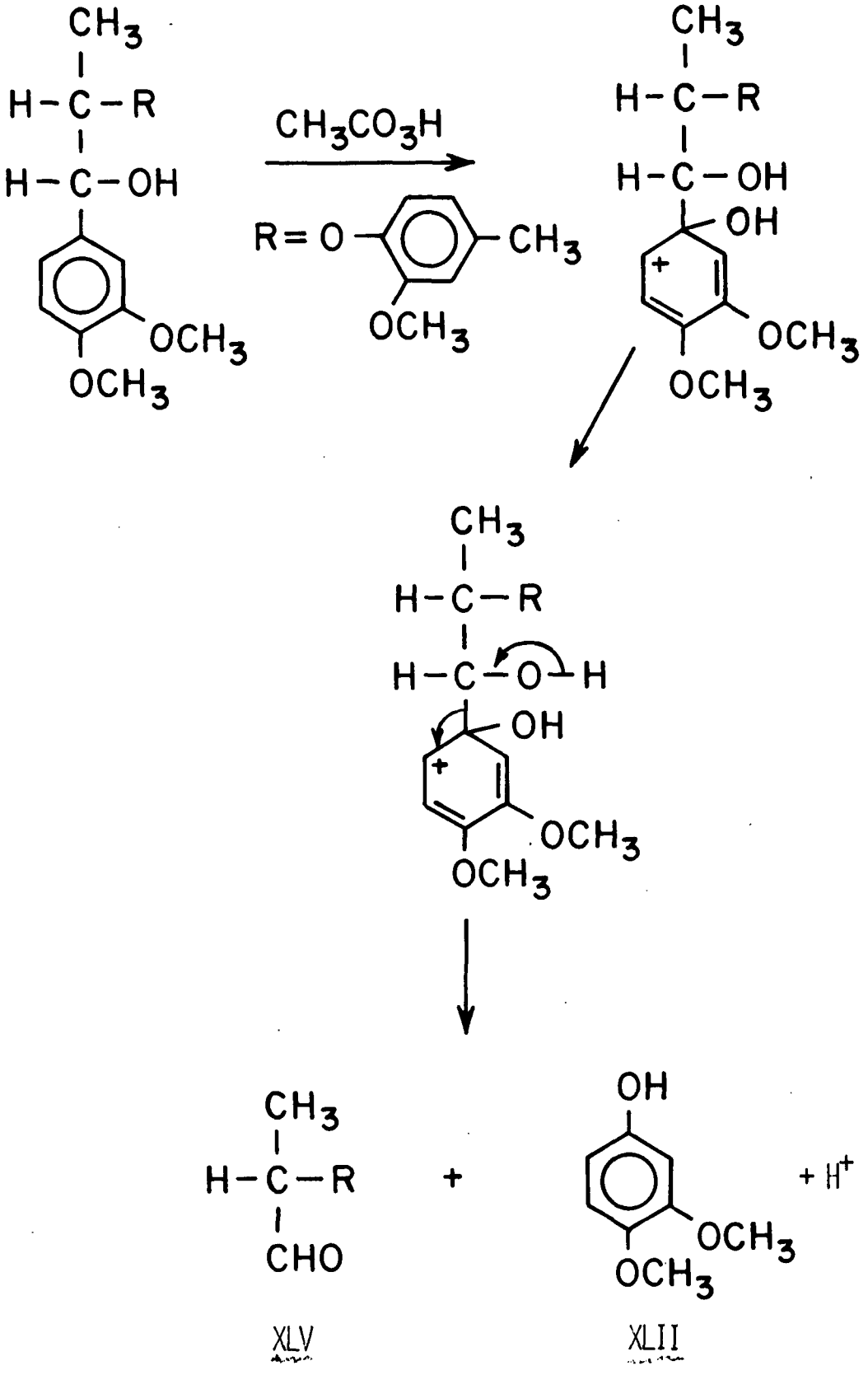


Figure 23. Possible Mechanism for Formation of Aldehyde XLV in the PA Oxidation of β-Ether XXXVI

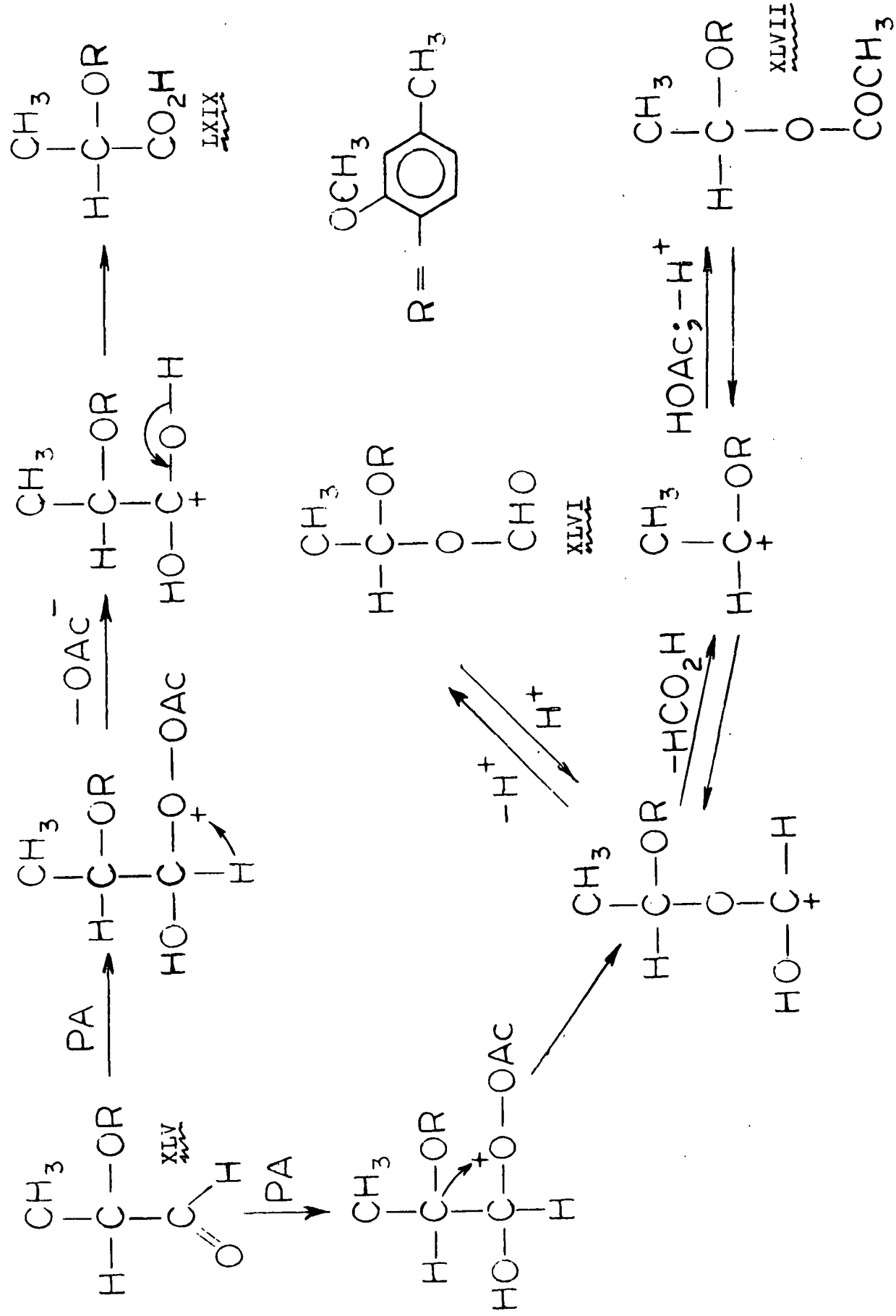


Figure 24. PA Oxidation of Aldehyde XLV

lead to the carboxylic acid LXIX or the hemiacetal formate XLVI. The hemiacetal formate XLVI undergoes transesterification to give the hemiacetal acetate XLVII due to the large excess of acetic acid in the reaction medium used in this study. The finding of the hemiacetal formate in this study is the first reported identification of this type of oxidation product and provides proof of the existence of the intermediary hemiacetal formate in the reactions leading to the hemiacetal acetate XLVII from the aldehyde XLV.

While the yield of these oxidation products was less than that reported by Sakai, et al. (31) there are several factors that may have caused the differences noted. In addition to a difference in reaction media employed there are two major differences in the type of model compound used that would affect the relative yields of these oxidation products. The high yields reported by Sakai, et al. (31) were obtained in the PA oxidation of 1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)ethanol. In this model the substituent para to the side chain is hydroxy and not methoxy as was used in this study. The difference in electron donating abilities of these two groups as measured by the σ_p values are -0.37 for hydroxyl and -0.27 for methoxyl (16). In view of the large negative ρ values associated with electrophilic aromatic subsitution reactions (ρ = -4 to -8 for many aromatic electrophilic substitution reactions (16)) a greater reactivity is expected from a p-hydroxyl as compared to a p-methoxyl. Similarly, the use in this study of a more electron donating p-methyl group in the creosol ring will enhance the relative reactivity of the substrate at this position as well as cause greater reactivity of the oxidation products.

BENZYLIC HYDROXYL OXIDATION, OXIDATION PATH D

The mechanism for the formation of XXXVII in the PA oxidation of β-ether XXXVI is not readily apparent. While there have been reports of peroxyacid

oxidation of secondary alcohols to ketones in the literature (41,42), this type of reaction is usually of minor importance. The information available seems to indicate that this reaction is due to a radical mechanism. Rapson and Strumila (43) proposed that oxidation of vanillyl alcohol by PA under neutral conditions was the result of reaction with hydroperoxy free radicals supplied by the homolysis of hydrogen peroxide. It is also of interest that Hatakeyama, et al. (44) reported no free radical formation during the PA oxidation of barium vanillylsulfonate, but using vanillyl alcohol as a substrate, free radicals could be detected. It is therefore proposed that the reaction of β-ether XXXVI to XXXVII proceeds by an undetermined route that may involve a free radical mechanism.

While this reaction does not lead directly to cleavage of the β-aryl ether linkage between the two aromatic systems, it does provide a carbonyl function which is very easily oxidized by PA to an ester. Subsequent hydrolysis of the ester formed does lead to cleavage of the ether linkage between the two aromatic rings.

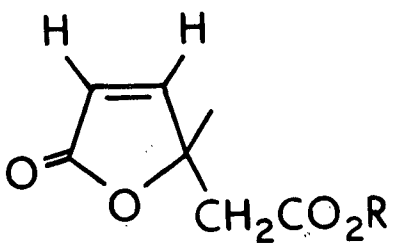
DEMETHOXYLATION AND RING HYDROXYLATION, OXIDATION PATH E

The occurrence of demethoxylation and ring hydroxylation of β-ether XXXVI and its oxidation products was confirmed by the isolation and identification of oxidation products L-LIII, LVI-LIX and LXII and LXIII. These findings agree with those previous workers (29-31). The finding of a significant amount and quantity of products in the PA oxidation of β-ether XXXVI having the veratryl (3,4-dimethoxyphenyl) type of substitution is in contrast to the findings reported by Oki, et al. (29,30). They had proposed that a veratryl type β-aryl ether was demethoxylated to a guaiacyl (4-hydroxy-3-methoxyphenyl) or catechol (3,4-dihydroxyphenyl) type of β-ether product prior to other types of oxidation reactions. Although there is the difference in reaction media and the activating effect of the methyl

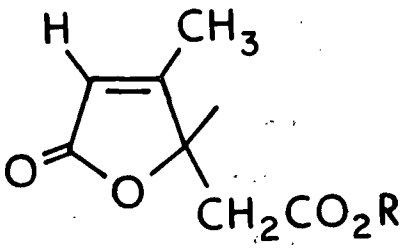
group toward cleavage of the β-aryl ether bond, it seems questionable that removal of one or both of the veratryl methoxy substituents is necessary for cleavage of the interaryl linkage by the oxidation routes indicated in this study. Due to the increased reactivity of the demethoxylation and ring hydroxylation products, the number and amounts of such products identified in this study is very likely to be low as a result of subsequent oxidation.

RING CLEAVAGE TO MUCONIC ACIDS

The isolation and identification of oxidation product LX in the PA oxidation of β-ether XXXVI is very interesting because it suggests that the PA oxidation of creosol does not necessarily go strictly by way of the 4-methyl-o-benzoquinone (VI) as previously suggested by Farrand (19). The inclusion of the ring methyl group verifies the origin of this product to be the creosol ring in the starting material, β-ether XXXVI. Farrand has previously shown that 3-methylmuconic acid can form both lactones LX and LXX and that LXX is the preferred lactonization product of cis,trans-3-methylmuconic acid.



LX



LXX

It should be noted that retention of the methoxy methyl group in a monomethyl ester in the PA oxidation of creosol can only lead directly to lactone LX. A possible mechanism for the formation of LX is shown in Fig. 25. While it is possible that there may be transesterification or esterification from the methanol released upon cleavage of the methoxyl groups, it seems fortuitous that

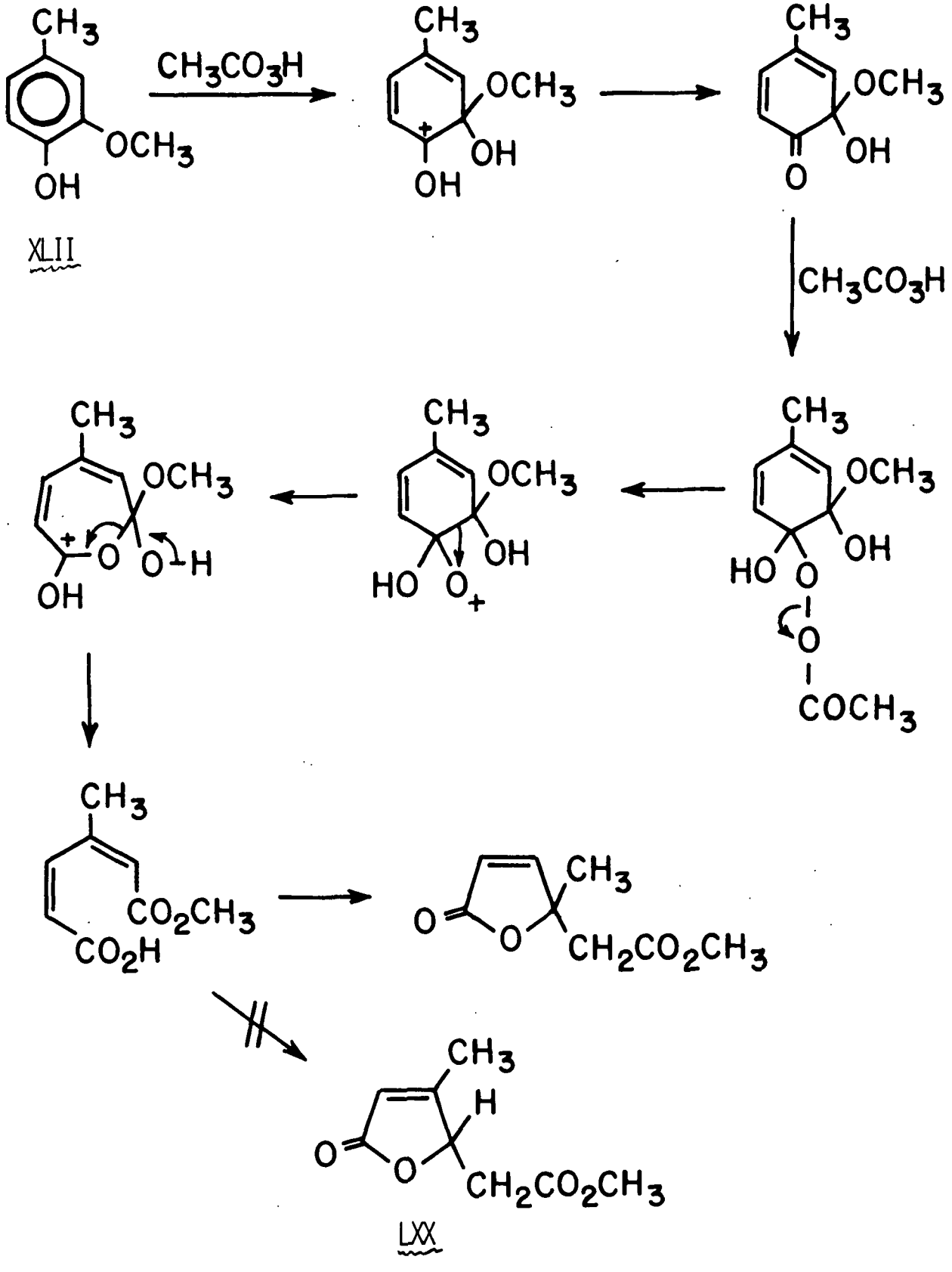


Figure 25. PA Oxidation of Creosol (LIV)

only lactone LX and not the preferred lactone LXX was found. Similar PA oxidation with retention of the methoxyl group in this manner agrees with the results of Hatakeyama, et al. (24) as previously described.

QUALITATIVE ANALYSIS OF OXIDATION PRODUCTS

Preliminary oxidations showed that in addition to the two major PA oxidation products of β-ether XXXVI, diol XL and creosol, there were a large number of minor oxidation products. To provide sufficient amounts of these minor oxidation products for identification purposes, approximately 0.01 mole of β-ether XXXVI was oxidized for 24 hours at 25°C. Due to the large number of oxidation products it was impractical to synthesize known compounds for comparison in all cases. The use of preparative GLC to obtain pure samples for PMR spectrometry proved to be very useful in determining the structures of the oxidation products in addition to the MS and GLC retention data.

The preliminary data showed that extraction of the neutralized oxidation samples with several volumes of ether did not cleanly fractionate diol XL as a considerable amount of this product was found in the acidic fraction. A continuous ether extraction did cleanly fractionate diol XL into the neutral and phenolic fraction. This technique was quite cumbersome and the aqueous solution showed a sharp increase in pH (from 7 to 9-10) after continuous extraction indicating the possibility of extraction of a significant amount of acidic compounds into the ether phase. A multiple chloroform extraction was then used that showed complete recovery (99%) of the diol XL through the workup procedure. While this procedure worked well for the quantitative product samples, the qualitative acidic fraction contained small amounts of a number of neutral and phenolic products due to the much larger sample size used. In addition to the extractive fractionation, the neutral-phenolic and acidic qualitative fractions were further fractionated

by the use of column chromatography on silica gel. This additional fractionation separated the large excess of starting material and the gas chromatograms of the various fractions were less complex, thus facilitating the preparative GLC collection and mass spectral analysis.

The methods used for identification of the PA oxidation products of β-ether XXXVI are given in Table III. The GLC retention times for these compounds are given in Table III.

TABLE III

IDENTIFICATION OF PA OXIDATION PRODUCTS OF β-ETHER XXXVI

Oxidation Product	Product[a] Structure	Proof of[b] Structure	Retention Time (min)
2-(2-Methoxy-4-methyl-phenoxy)propionaldehyde	XLV	1,2,4	24.5
1-(2-Methoxy-4-methyl-phenoxy)ethyl formate	XLVI	3,5	21.5
1-(2-Methoxy-4-methyl-phenoxy)ethyl acetate	XLVII	3,5	25.5
Erythro 1-(3,4-dimethoxy-phenyl)propan-1,2-diol	XLa	1,2,5,6,8	37.0
Threo 1-(3,4-dimethoxy-phenyl)propan-1,2-diol	XLb	1,3	38.5
1-Acetoxy-1-(3,4-dimethoxy-phenyl)propan-2-ol	XLVIII	3,5	45.5 47.5
2-Acetoxy-1-(3,4-dimethoxy-phenyl)propanol	XLIX	3,5	44.5
1-(3,4-Dimethoxyphenyl)-1-hydroxypropan-2-one	XLI	1,2,5	40.0
3,4-dimethoxybenzaldehyde	XLIV	1,2,4	30.0
3,4-Dimethoxyphenol	XLII	1,2,5	21.5
3,4-Dimethoxyphenyl acetate	LIII	1,2,4	23.0
1,4-Diacetoxy-2-methoxy-hydroquinone	L	1,2,4	36.5
3,4-(Acetoxy,methoxy)phenol	LII	3,5	31.0

See end of table for footnotes.

TABLE III (Continued)

IDENTIFICATION OF PA OXIDATION PRODUCTS OF β-ETHER XXXVI

Oxidation Product	Product[a] Structure	Proof of[b] Structure	Retention Time (min)
2-Methoxy-4-acetoxy or 2-methoxy-5-acetoxy phenol	LIII	3,5	34.0
2-Methoxy-4-methylphenol	LIV	1,2,4,5	12.9
2-methoxy-4-methyl-phenyl acetate	LV	1,2,4	16.5
2-Acetoxy-4-methylphenol	LVI	3,5	18.0
2-Acetoxy-5-methylphenol	LVII	3,5	18.5
2-Methoxy-4-methyl-5-acetoxy-phenol	LVIII	3,5	32.0
2-Methoxy-4-methyl-5-acetoxy-phenyl acetate	LIX	3,5	32.5
5-Carboxymethyl-4-methyl-2-(5H)-furanone	LX	2,4[c]	N.D.
cis,trans-3-Methylmuconic acid	LXI	1,2	32.0
3',4'-Dimethoxy-2-(2-methoxy-4-methylphenoxy)propiophenone	XXXVII	1,2,7	88.0
See footnote d	LXII	3,5	91.5
See footnote d	LXIII	3,5	94.0

[a] Structures shown in Fig. 16.

[b] Proof of structure as follows:

1. GLC retention time comparison with known sample or TMS derivative thereof.
2. Mass spectral comparison with known sample or TMS derivative thereof.
3. Mass spectrum of oxidation product or TMS derivative thereof — known unavailable.
4. PMR spectral comparison with known sample.
5. PMR spectrum of oxidation product or TMS derivative thereof.
6. Melting point — comparison made with literature value.
7. TLC color reaction and R_f value comparison with known sample.
8. Infrared spectral comparison with known sample.

[c] Known not available — comparison was made with reported value (19).

[d] Exact structure could not be rigorously proven with data.

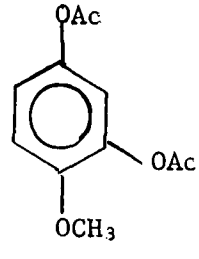
OXIDATION PRODUCTS FOR WHICH KNOWNS WERE AVAILABLE

The majority of the oxidation products were identified by comparison of the PMR and mass spectra of the oxidation products and known samples or TMS derivatives thereof. The PMR spectra are given in Appendix I and the mass spectra of the oxidation products and known samples are compared in Appendix II.

In addition to the GLC retention time, mass spectral and PMR data, the major oxidation product, diol XLa, was also characterized by comparison of its infrared spectrum and melting point with that of the known erythro diol XLa. The melting point (122-123°C) confirmed the erythro configuration. The infrared spectra are compared in Fig. 26 and the fit is very good thus further confirming the structure.

The assignment of the threo configuration to oxidation product XLb is based primarily on the comparison of the mass spectra of the bis-TMS ether of XLb and the bis-TMS ether of a known sample of XLa which were identical as shown in Fig. 27. This comparison eliminates the possibility that this peak represented a mono-TMS ether. In addition, the retention times of the TMS ether of XLb matched that of a minor impurity in the gas chromatograph of the bis-TMS ether of the known sample of XLa. The slightly greater retention time of the threo isomer has been previously reported for similar compounds (45).

The GLC retention time, PMR and mass spectral data for oxidation product L were identical with that of a known sample of di-O-acetylmethoxy-p-hydroquinone. Due to the lack of a sample of 2,4-diacetoxy-1-methoxybenzene LXXI there is a



LXXI

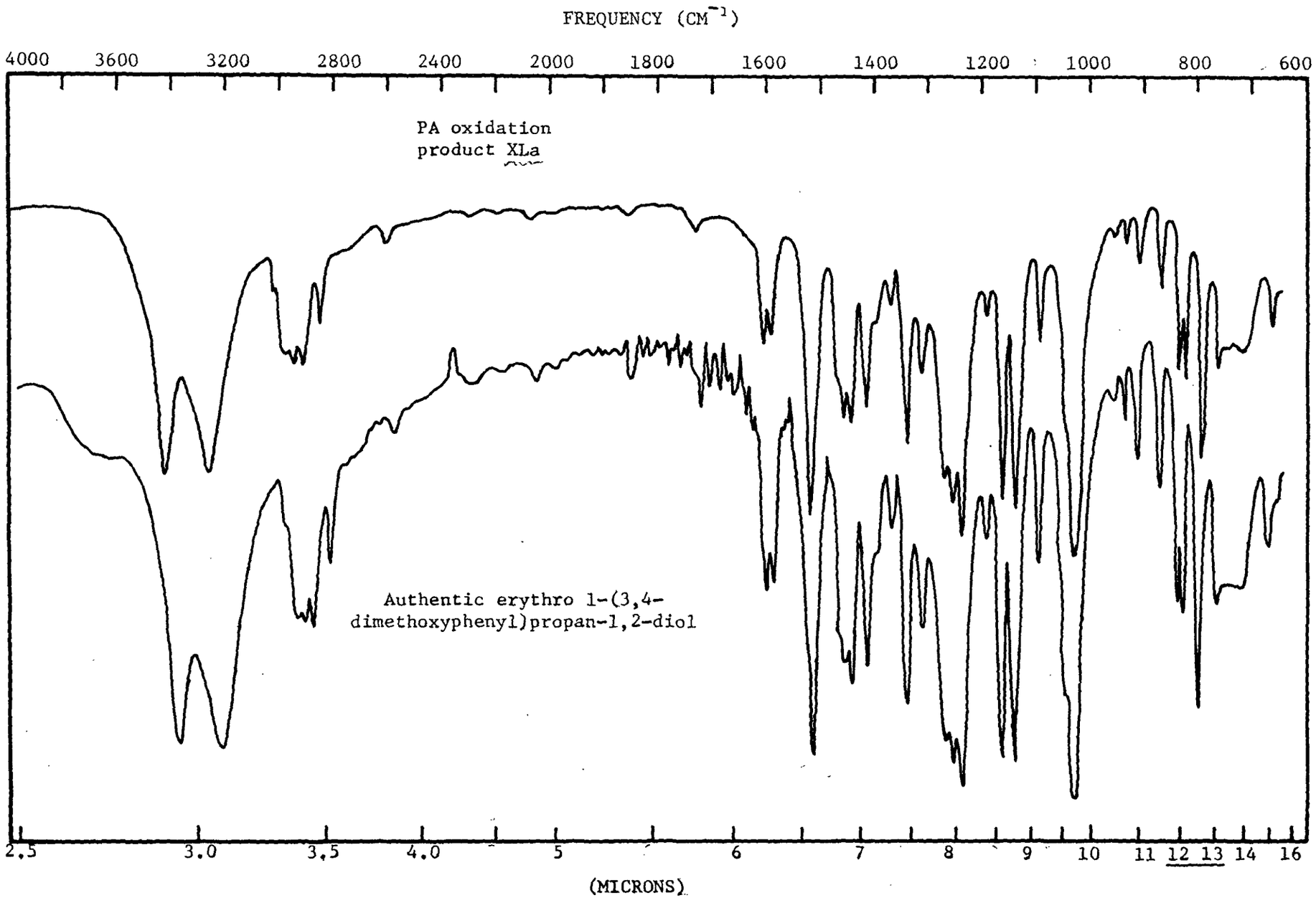
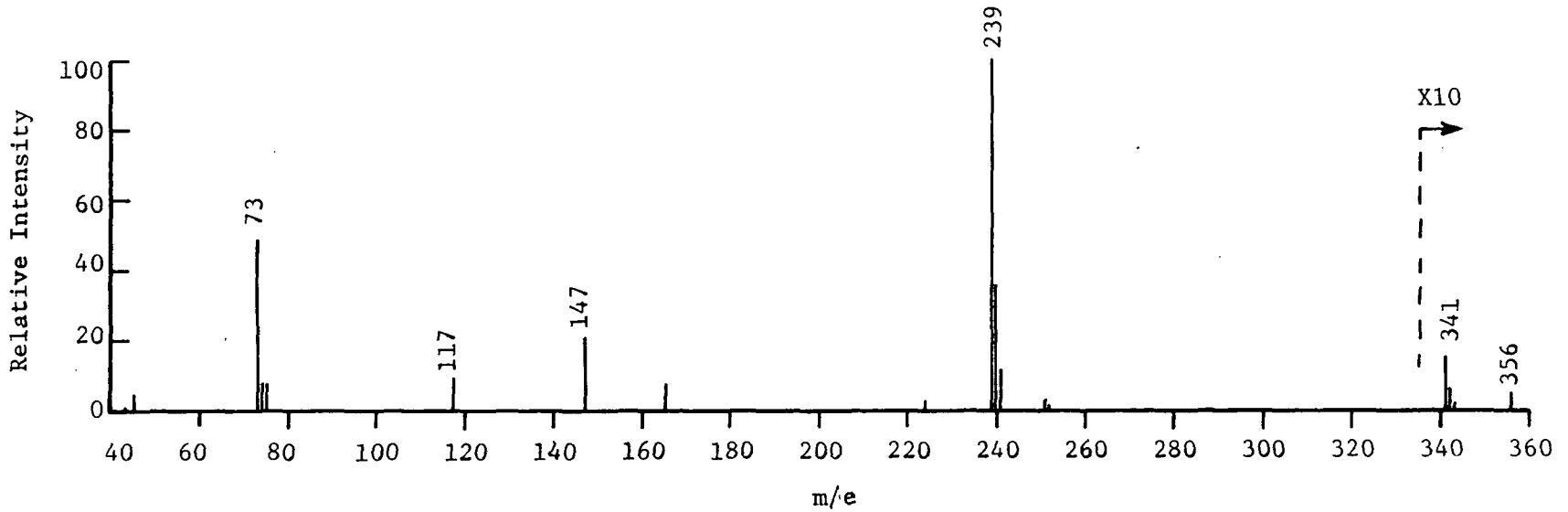
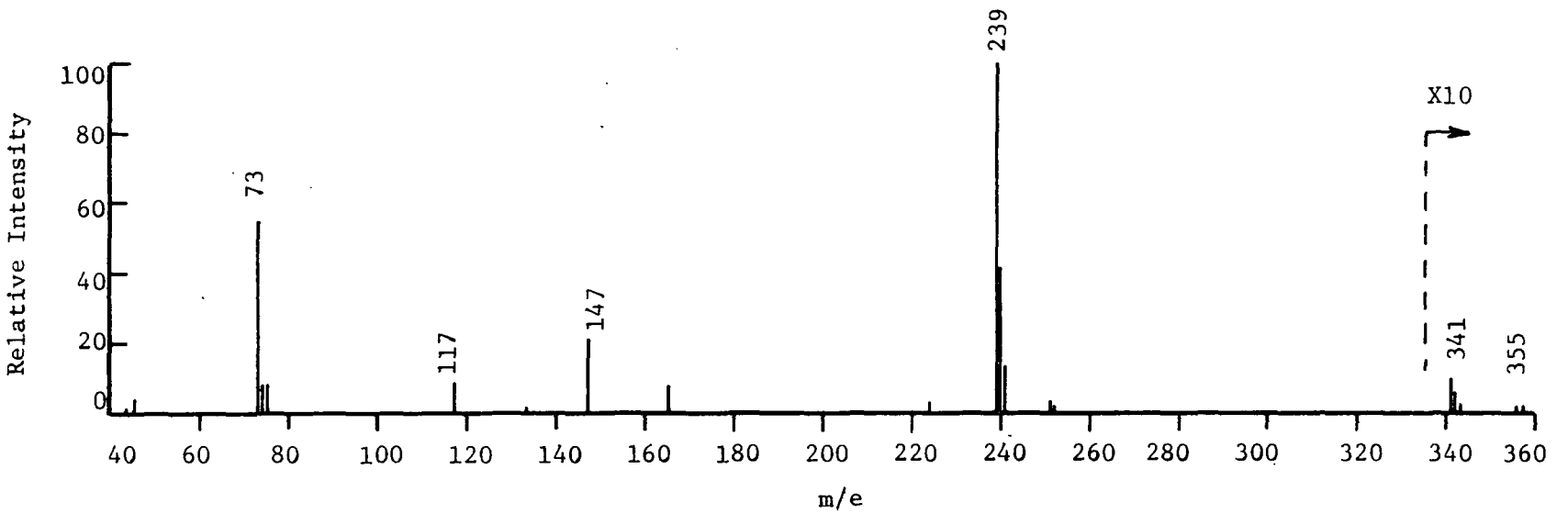


Figure 26. Comparison of IR Spectra of Oxidation Product XLa and Authentic Sample of XLa



Mass spectrum of bis-TMS ether of oxidation product XLb



Mass spectrum of TMS derivative of 1-(3,4-dimethoxyphenyl)-propan-1,2-diol

Figure 27. Mass Spectra of bis-TMS Ethers of Known Sample of XLa and Oxidation Product XLb

possibility that the GLC retention and mass spectral data could be inconclusive in eliminating LXXI as a possible structure. The aromatic region of the PMR spectra for known L and oxidation product L are given in Fig. 28. It can be seen that the chemical shifts are identical in this region. These data, in addition to the retention time and mass spectral data, thus confirm the structure of oxidation product L as di-O-acetylmethoxy-p-hydroquinone.

The mass spectra of the TMS ether of β-aryl ether XXXVI and an authentic sample of the keto β-ether XXXVII are shown in Fig. 29. There are several key differences in the mass spectra of these two compounds, most noticeably the peaks at m/e 330, 194, 165, and 138 which are weak or absent in the MS of the TMS ether of XXXVI but strong in the MS of XXXVII. The MS of β-ether XXXVI shows strong peaks at m/e 239, 267, and 73 that are weak or absent in the MS of XXXVII. In Fig. 30 are shown the mass spectra of a known sample of XXXVII and PA oxidation product XXXVII. The large peaks at m/e 404, 239 and 73 indicate the presence of the TMS ether of β-ether XXXVI. This was unavoidable because the sample had a very large excess of starting material and the peak for XXXVII was a small peak on the tail of the peak for the TMS derivative of β-ether XXXVI. The peaks at m/e 330, 194, 165 and 138 do offer good evidence for the presence of XXXVII. In addition to this, the GLC retention time for the authentic sample of XXXVII and the oxidation product XXXVII was identical. The R_f values for the thin-layer chromatograms of the known and oxidation product samples of XXXVII using 50:50 isopropyl ether:ethyl ether as developing solvent were identical as were the color reactions with methanolic sulfuric acid and 2,4-dinitrophenylhydrazine spray reagents. Due to the small size for peak XXXVII it was not practical to isolate a sample of pure XXXVII by preparative GLC. It is concluded from the above data that PA oxidation product XXXVII is 3',4'-dimethoxyphenyl-2-(2-methoxy-4-methylphenoxy)propiophenone.

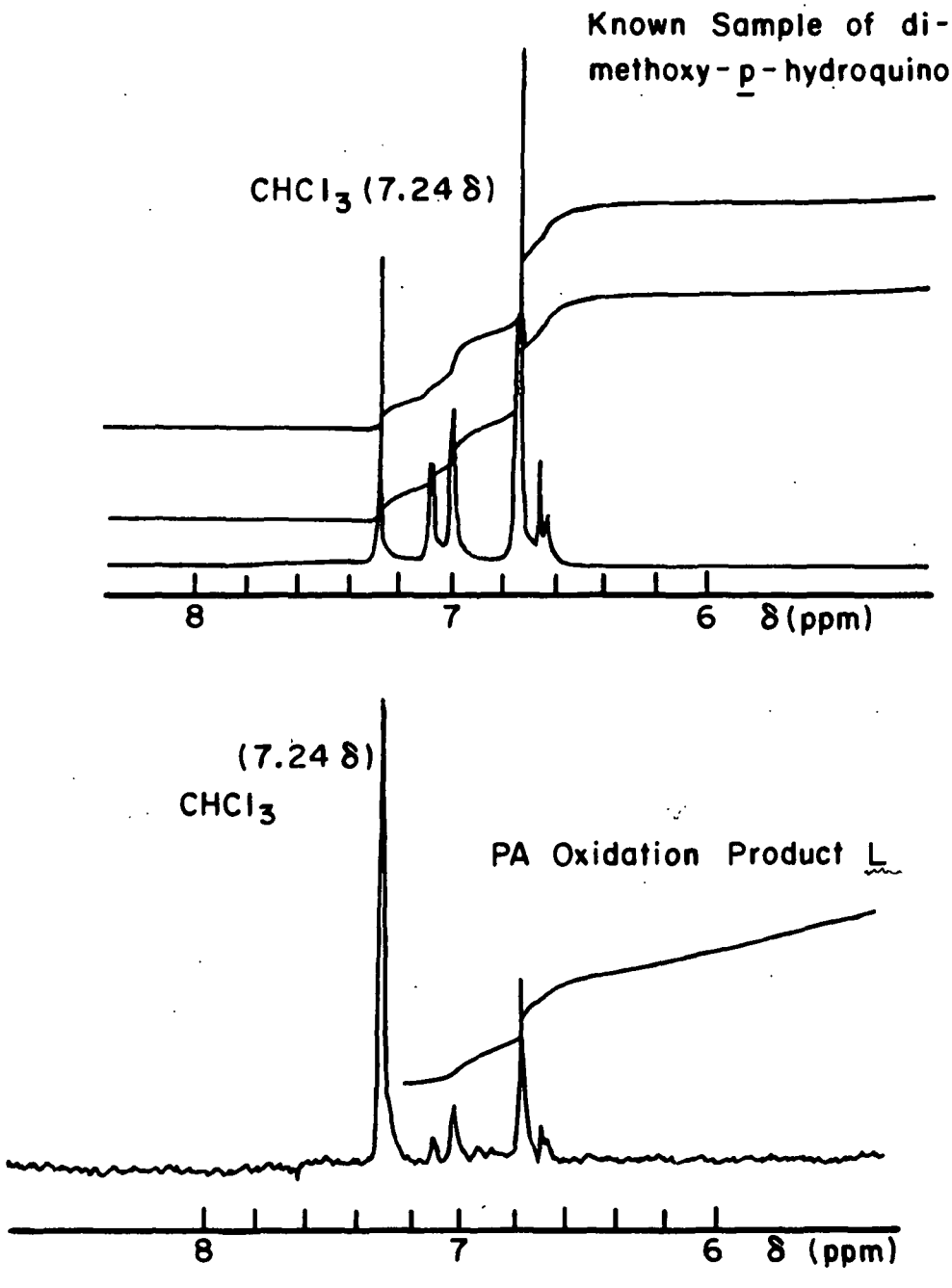
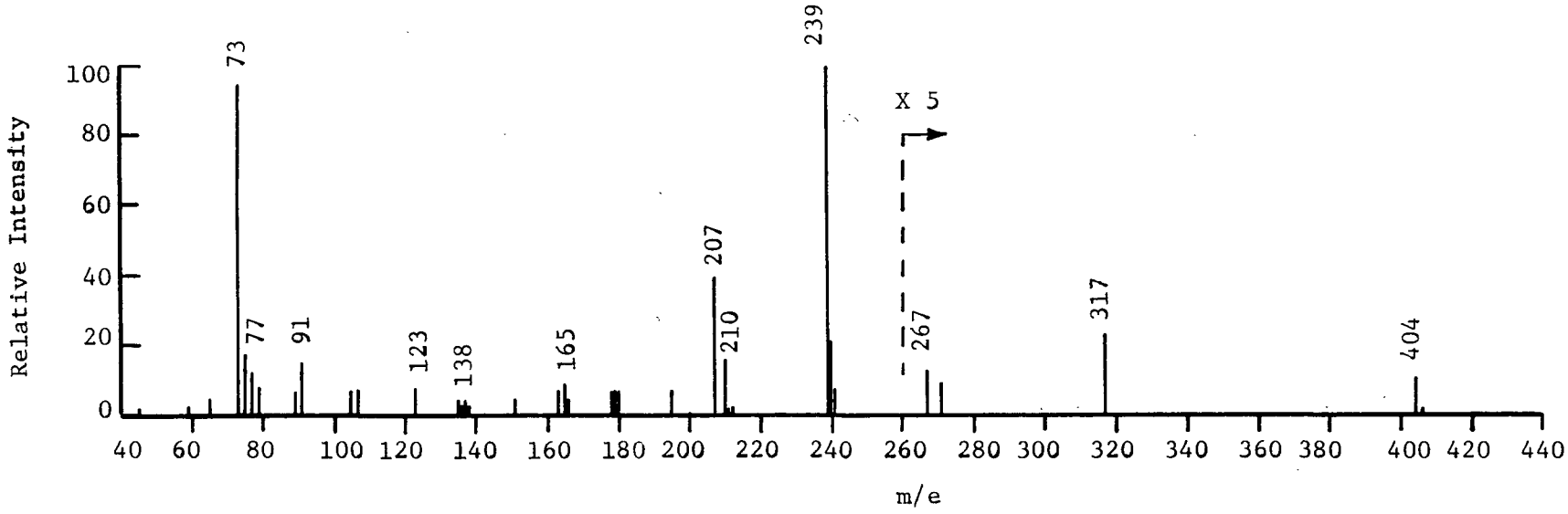
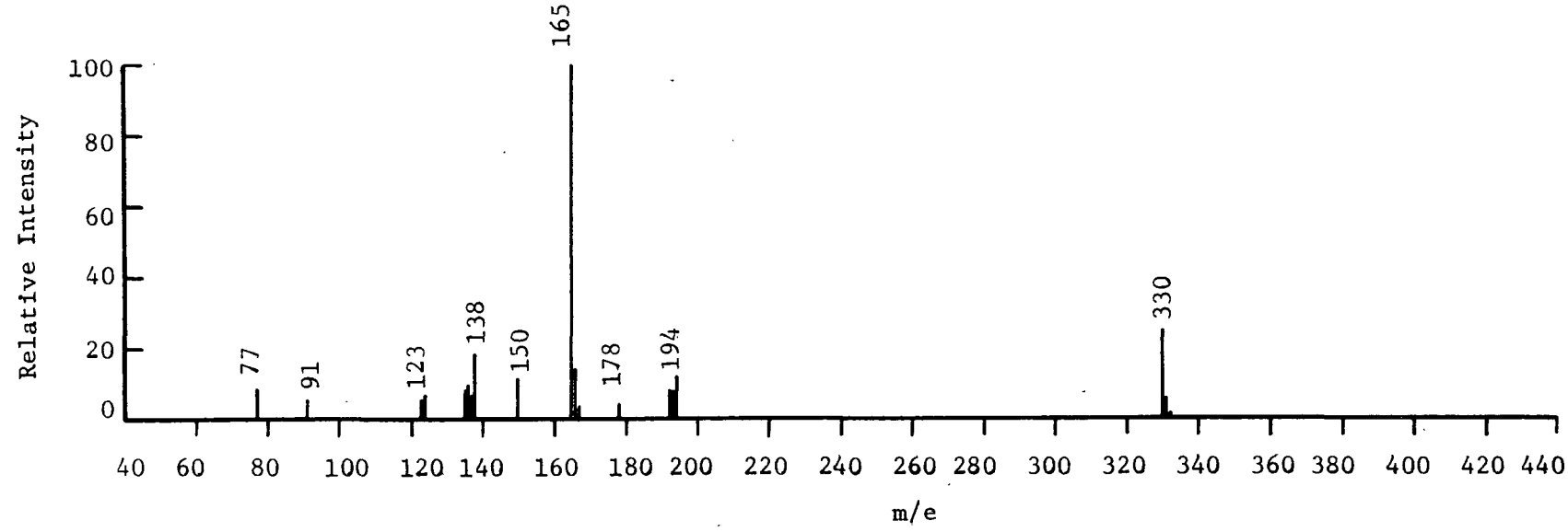


Figure 28. PMR Spectral Comparison of L and Known Sample

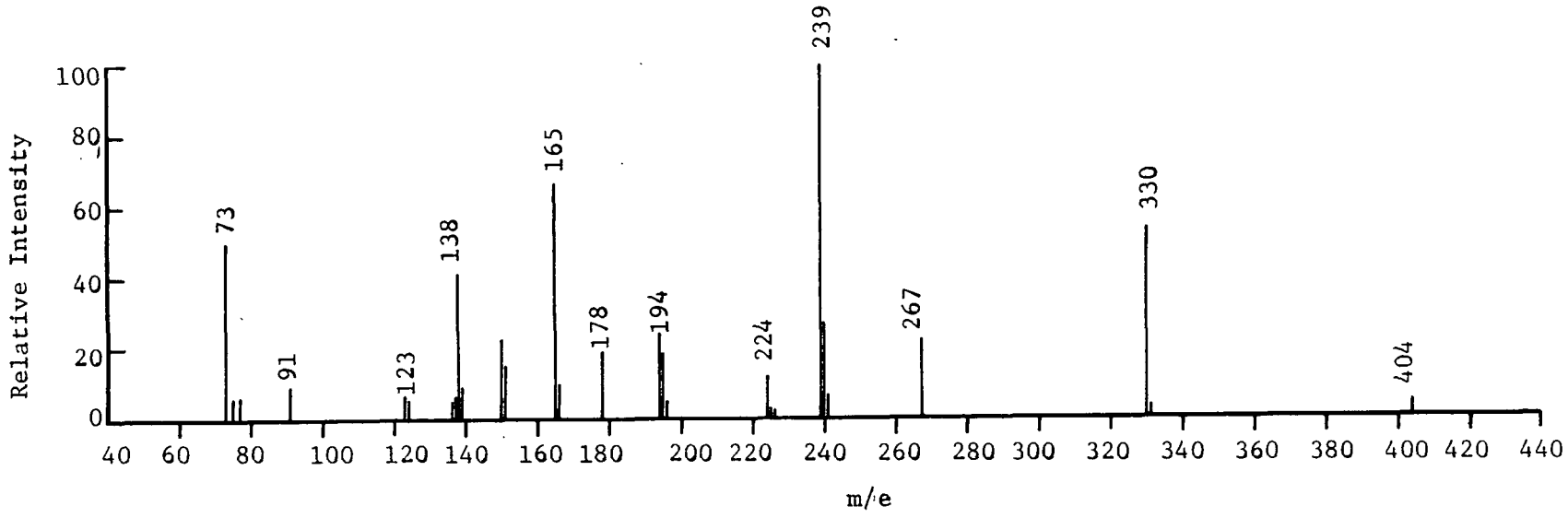


Mass spectrum of TMS derivative of beta-ether XXXVI

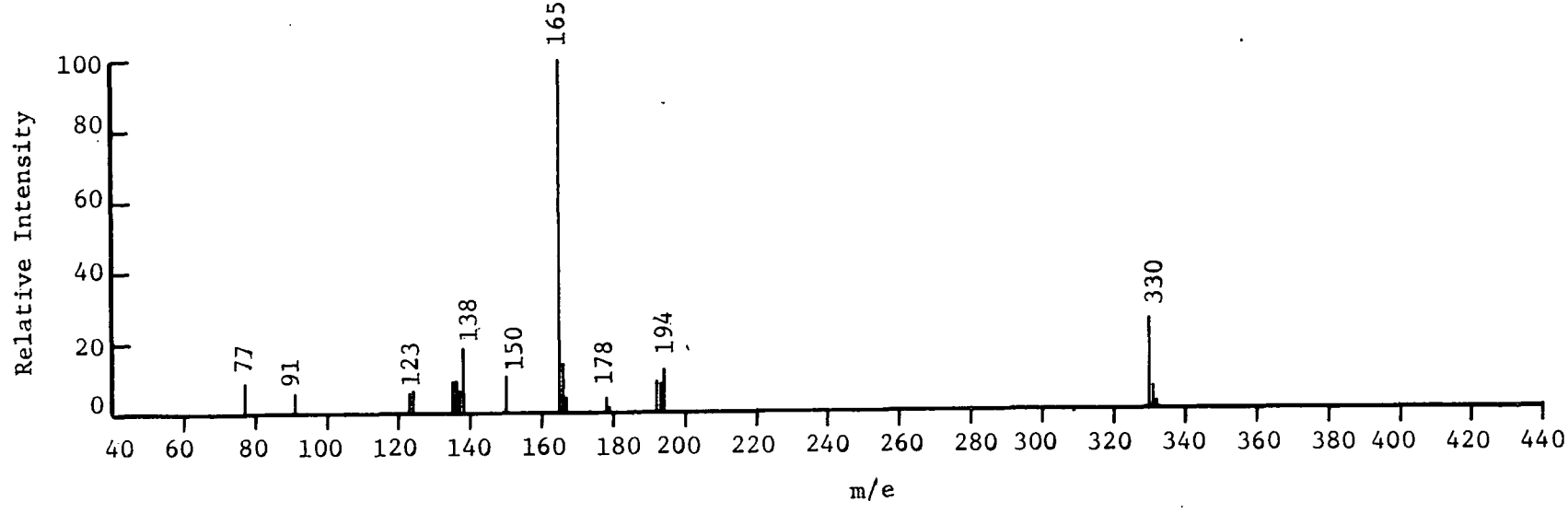


Mass spectrum of 3',4'-dimethoxy-2-(1-methoxy-4-methylphenoxy)propiophenone

Figure 29. Mass Spectra of Known Samples of XXXVII and TMS Ether of XXXVI



Mass spectrum of oxidation product XXXVII



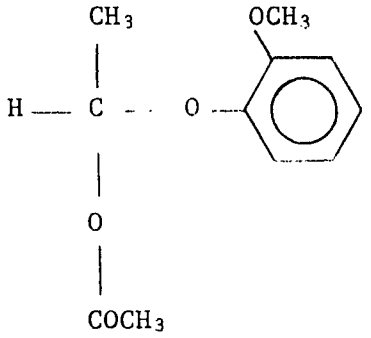
Mass spectrum of 3',4'-dimethoxy-2-(1-methoxy-4-methylphenoxy)propiophenone

Figure 30. Mass Spectra of Oxidation Product XXXVII and Known Sample of XXXVII

OXIDATION PRODUCTS FOR WHICH KNOWNS WERE NOT AVAILABLE

1-(2-Methoxy-4-methylphenoxy)ethyl Acetate (XLVII)

A similar product, 1-(2-methoxyphenoxy)ethyl acetate (LXXII) had been previously reported by Sakai, et al. (31) in the PA oxidation of model compounds as discussed previously.



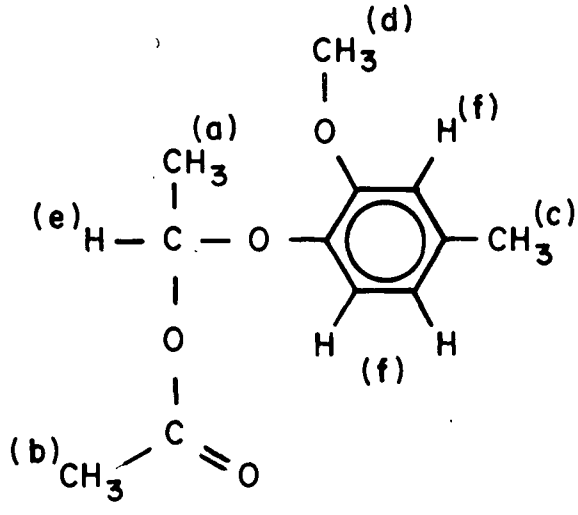
LXXII

The PMR spectrum and mass spectral fragmentation pattern for oxidation product XLVII are given in Fig. 31. Comparison is made between the major diagnostic mass spectral peaks found for LXXII by Sakai, et al. (31) and those found for XLVII in this study in Table IV showing good correlation between the two spectra. The complete mass spectrum is shown in Fig. 32. Also shown is the spectrum of the corresponding formate (see next section). Comparison of the PMR peaks also shows good correlation as seen in Fig. 31. The major differences are the aromatic methyl proton signal in XLVII at 2.29 δ and a difference of 1 proton in the multiplet aromatic proton signal. It is of interest to note the chemical shift of the methine proton at 6.39 δ. This is quite far downfield and is indicative of the strong deshielding caused by both the acetyl and phenoxy groups attached to this carbon atom. Based on the PMR and mass spectral data and their correlation to that of LXXII as reported by Sakai, et al. (31), the structure assigned to PA oxidation product XLVII is 1-(2-methoxy-4-methylphenoxy)ethyl acetate.

Structure and PMR Spectrum of Oxidation Product XLVII

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
a)	1.62(1.65)	Doub.	5	3
b)	2.01(2.02)	Sing.	-	3
c)	2.29(NA)	Sing.	-	3
d)	3.83(3.86)	Sing.	-	3
e)	6.39(6.49)	Quart.	5	1
f)	6.6-6.9	Mult.	-	3

Values given in parentheses are those for 1-(2-methoxyphenoxy)-ethyl acetate as reported by Sakai, et al. (31)



Mass Spectral Fragmentation Pattern for Oxidation Product XLVII

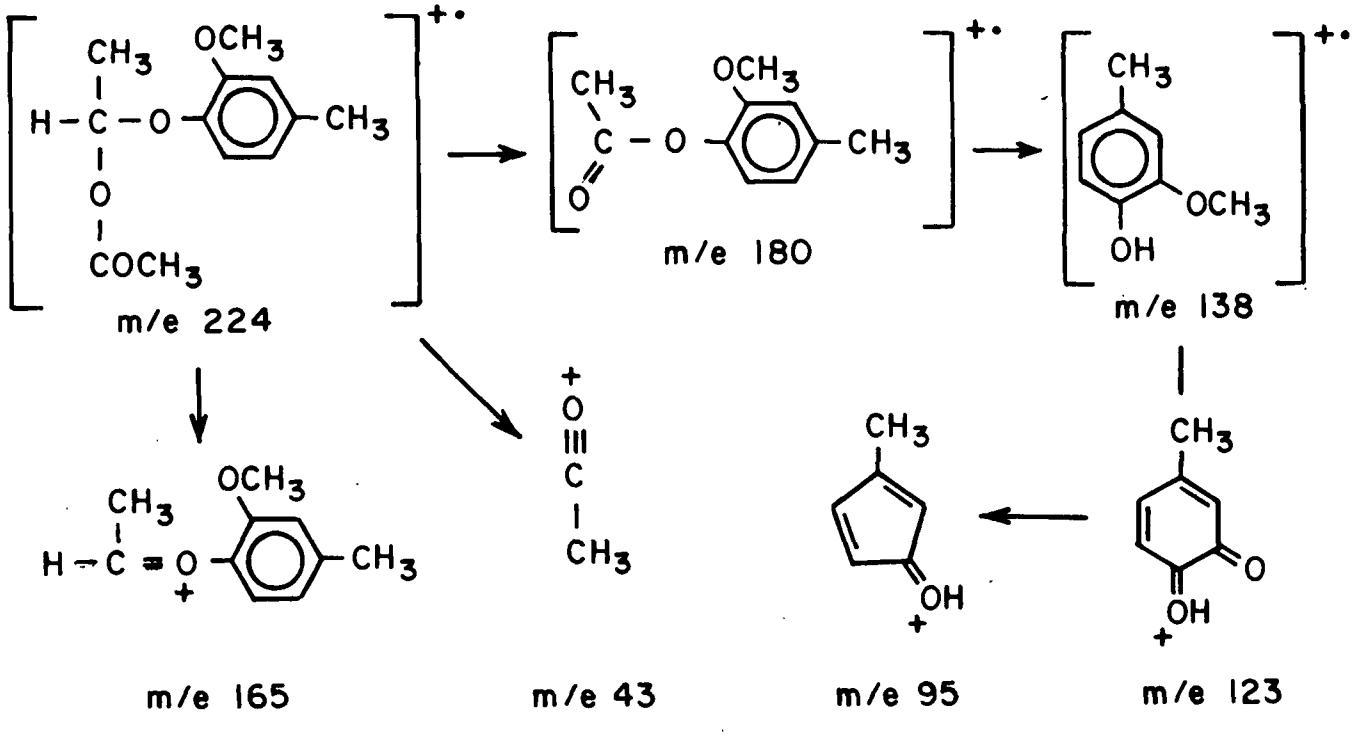


Figure 31. Mass Spectral Fragmentation Pattern and PMR Spectrum for Oxidation Product XLVII

TABLE IV

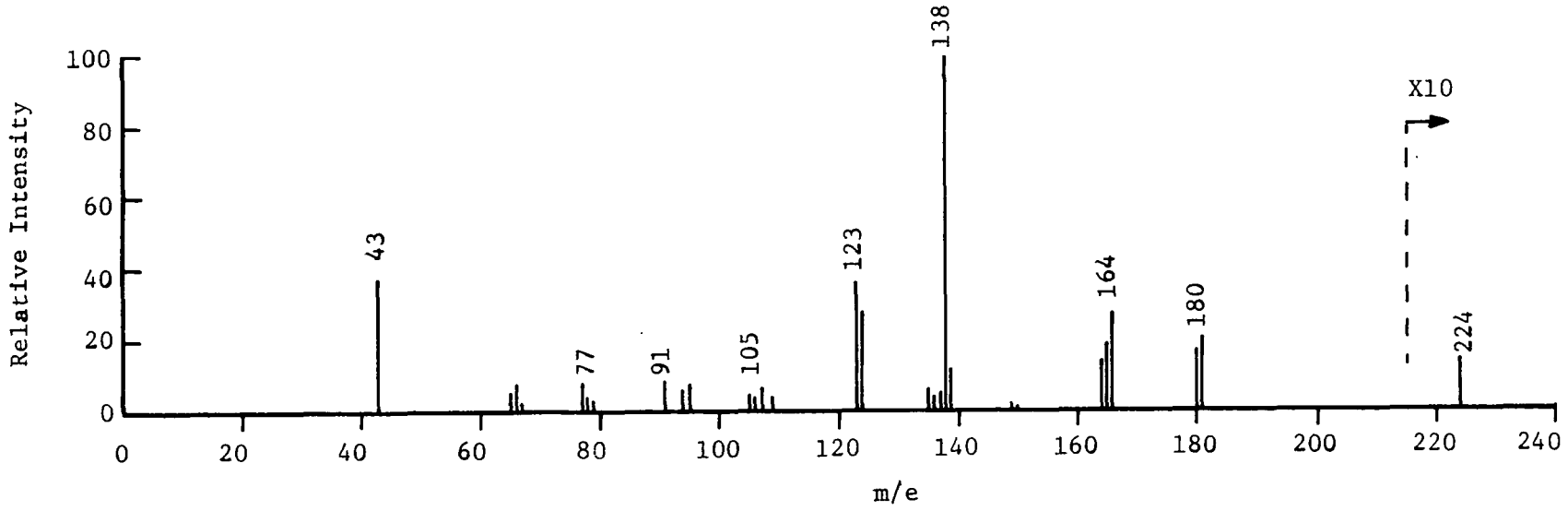
MASS SPECTRAL PEAK COMPARISON OF LXXII AND XLVII

Mass Spectral Peak	Relative Intensity (%) LXXII (31)	XLVII
M	10	1.4
M-44	15	16.1
M-59	23	18.6
M-86	100	100.0
M-101	38	35.8
m/e 43	63	37.2

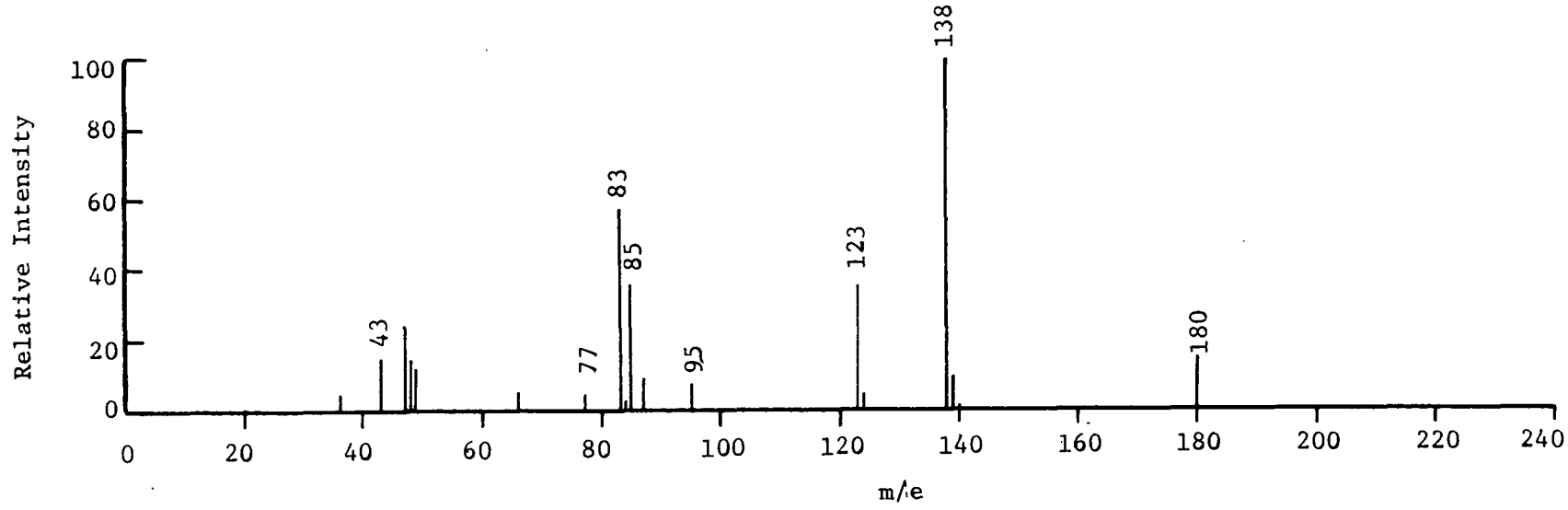
1-(2-Methoxy-4-methylphenoxy)ethyl Formate (XLVI)

The PMR spectrum and mass spectral fragmentation pattern for oxidation product XLVI are given in Fig. 33. The parent ion was absent even at reduced ionization voltages, but its mass spectrum is very similar to oxidation product XLVII. Similar to XLVII, cleavage occurs at the aryl ether bond with a proton transfer to give the base peak at m/e 138. The mass spectrum of XLVI shows a peak m/e 180 indicating loss of formaldehyde similar to the loss of acetaldehyde from XLVII. There is, however, no analogous peak at m/e 165 indicative of loss of formyloxy as found in XLVII for loss of acetoxy (M-59). The mass spectra of XLVI and XLVII are compared in Fig. 32.

The PMR spectrum of oxidation product XLVI is very similar to that for XLVII. The noticeable change is the absence of the acetyl peak at 2.01 δ and the appearance of the formate proton singlet at 8.00 δ. This change clearly indicates the structure of this compound to be that of XLVI. The chemical shift and integral value of the formyl proton are in good agreement with typical values for this type of proton (46). This product had been postulated as a reaction product by Sakai (31), but this is the first time this product has been isolated and identified.



Mass spectrum of oxidation product XLVII

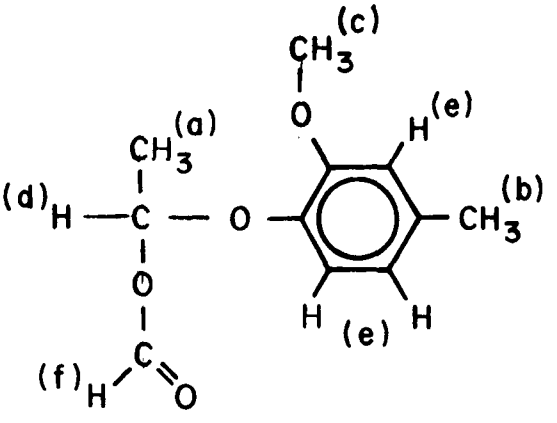


Mass spectrum of oxidation product XLVI

Figure 32. Mass Spectra of PA Oxidation of β-Ether XXXVI

Structure and PMR Spectrum of Oxidation Product XLVI

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
a)	1.66	Doub.	5	3
b)	2.31	Sing.	-	3
c)	3.84	Sing.	-	3
d)	6.50	Quart.	5	1
e)	6.7-7.0	Mult.	-	3
f)	8.00	Sing.	-	1



Mass Spectral Fragmentation Pattern for Oxidation Product XLVI

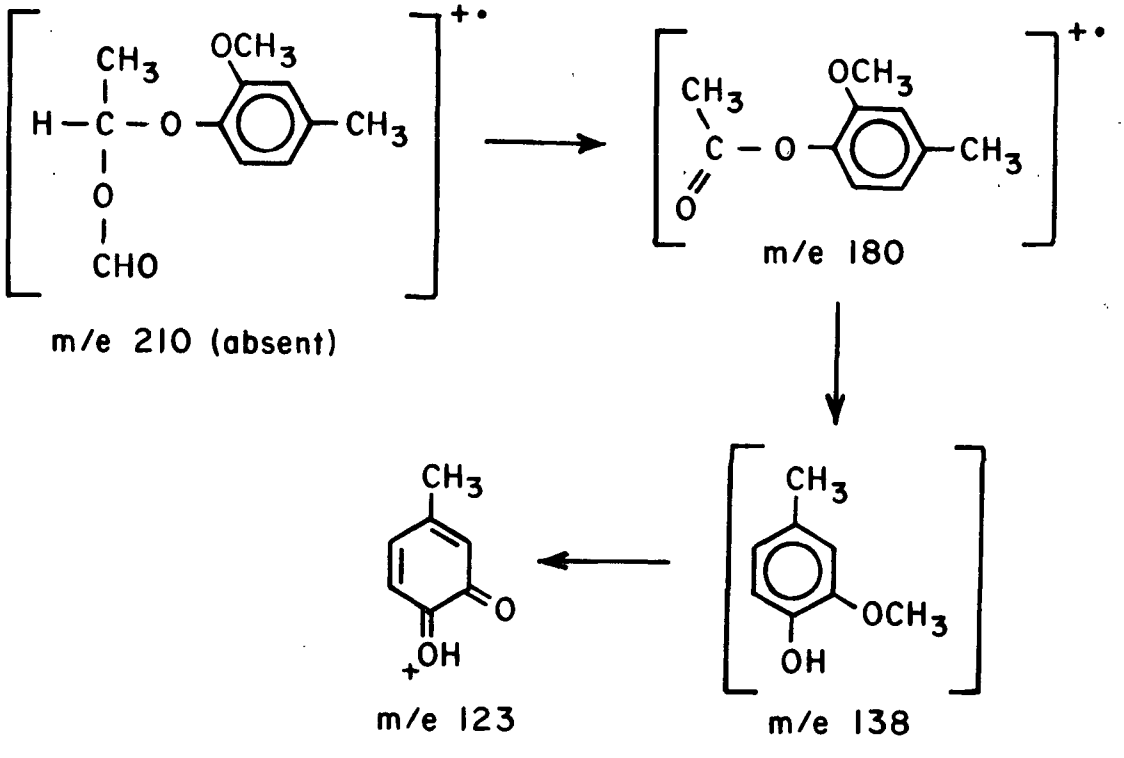
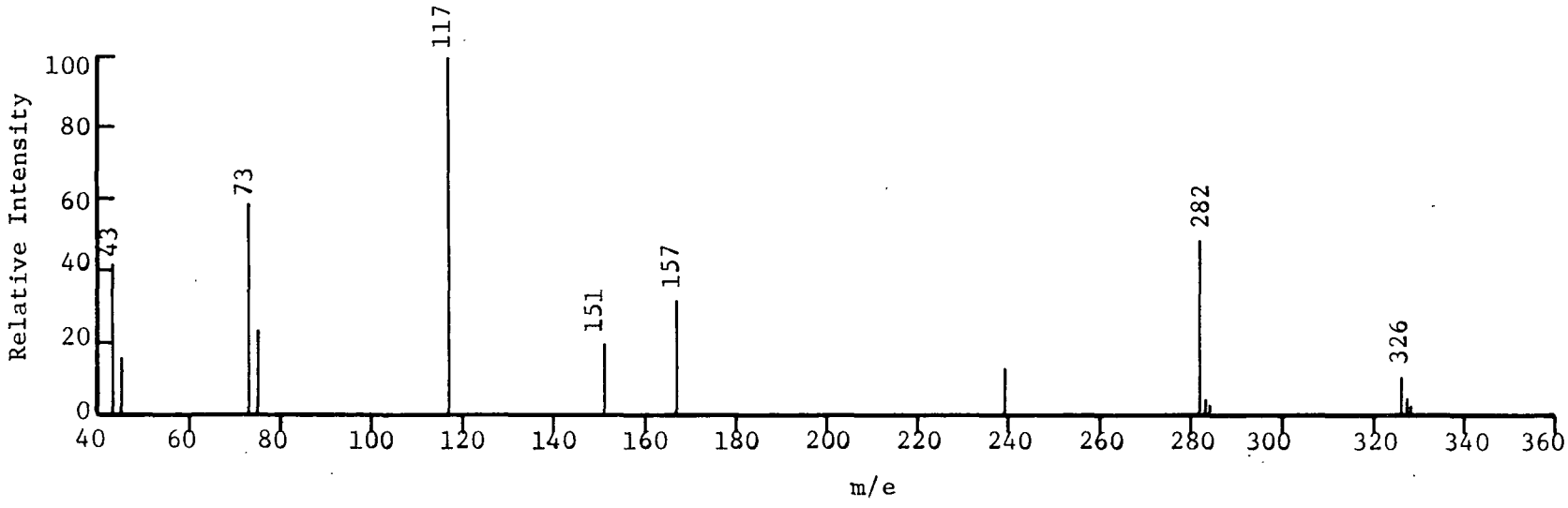


Figure 33. Mass Spectral Fragmentation Pattern and PMR Spectrum for Oxidation Product XLVI

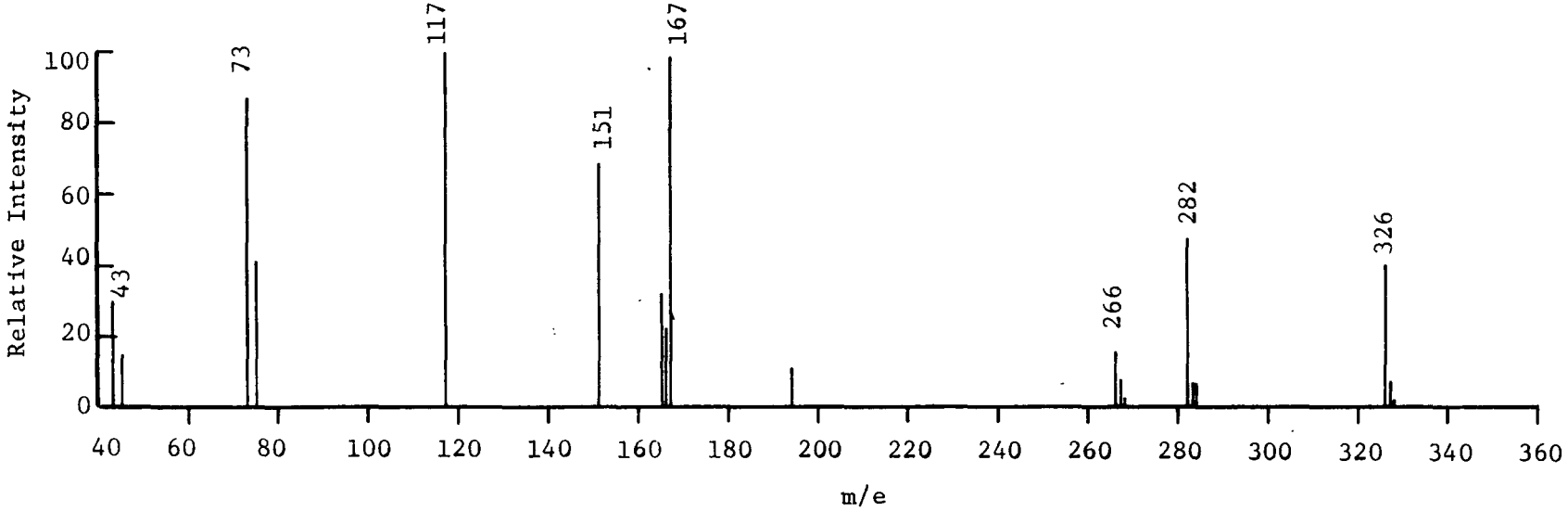
1-Acetoxy-1-(3,4-dimethoxyphenyl)propan-2-ol (XLVIII)

The mass spectra of the TMS derivatives of two PA oxidation products are shown in Fig. 34. These two products had unique but similar retention times in the gas chromatograph of the TMS derivatives of one of the later column chromatograph fractions. Their mass spectra suggested that they were likely to be very similar in structure. The peaks at m/e 73 and m/e 43 indicate that these compounds are trimethylsilyl derivatives and very likely also contain an acetyl group. It is not apparent that the peak at m/e 326 is the parent ion because trimethylsilyl derivatives usually show a much stronger peak at M-15 than for M (47).

The PMR spectrum and mass spectral fragmentation pattern for the derivatized products are shown in Fig. 35. The correct structure of these products becomes evident on examination of the PMR spectra. The presence of trimethylsilyl and acetyl groups are shown by the peaks at 0.01 and 2.08 δ, respectively. The peaks at 6.7-6.9 δ, 3.88 δ and 3.94 δ indicate a dimethoxyphenyl type structure. The side-chain proton signals at 1.12, 4.00 and 5.40 δ for the γ-, β- and α-carbon atom protons, respectively, complete the structural picture and indicate these products are trimethylsilyl ether-acetate ester derivatives of diol XL. The position of the two derivitizing functional groups are clearly indicated by the mass spectral and PMR data. The chemical shift of the proton on the α-carbon of the side chain, identifiable as a doublet, has been shifted 1.2 ppm downfield relative to the chemical shift of the same proton for the bis-trimethylsilyl ether of diol XL which was a doublet at 4.31 δ. The chemical shift of the proton on the β-carbon of the side chain, identifiable as a multiplet, has also been shifted downfield relative to the same proton in the bis-trimethylsilyl ether of diol XL but only by 0.15 δ. This indicated the acetyl group is substituted on the α-carbon atom and the strong deshielding of the acetyl group causes the large downfield shift of the chemical shift for the proton on the α-carbon atom. The presence of the acetyl group also causes a downfield shift for the chemical shift



Mass spectrum of TMS ether of oxidation product XLVIIIb

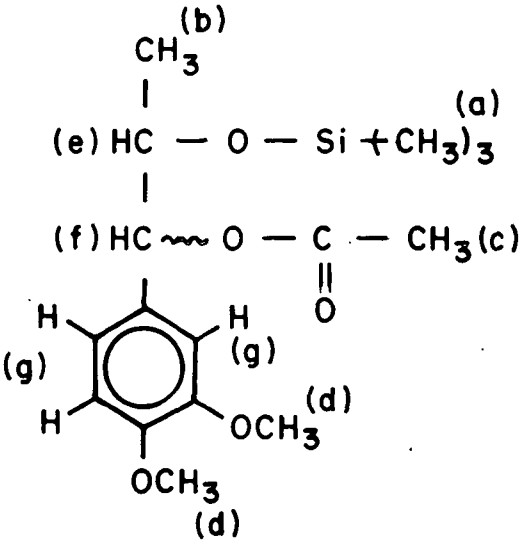


Mass spectrum of TMS ether of oxidation product XLVIIIa

Figure 34. Mass Spectra of TMS Ethers of Oxidation Products XLVIIIa and b

Structure and PMR Spectra

Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
XLVIIIa			
a) 0.01	Sing.	-	9
b) 1.12	Doub.	6	3
c) 2.08	Sing.	-	3
d) 3.88,3.94	Sing.	-	6
e) 4.00	Mult.	-	1
f) 5.40	Doub.	6	1
g) 6.7-6.9	Mult.	-	3
XLVIIIb			
a) 0.08	Sing.	-	9
b) 1.00	Doub.	7	3
c) 2.09	Sing.	-	3
d) 3.86,3.88	Sing.	-	6
e) 3.95	Mult.	-	1
f) 5.51	Doub.	6	1
g) 6.7-6.9	Mult.	-	3



Mass Spectral Fragmentation Pattern

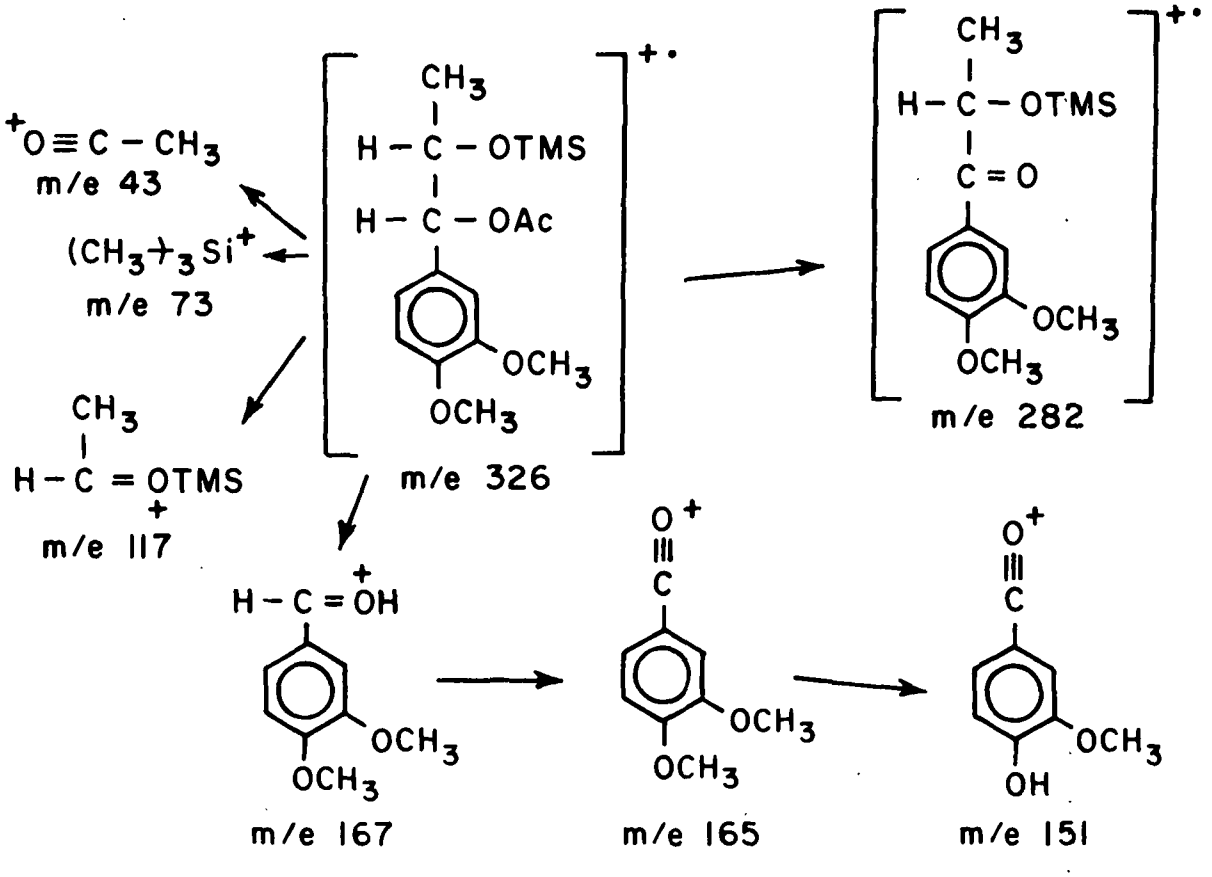


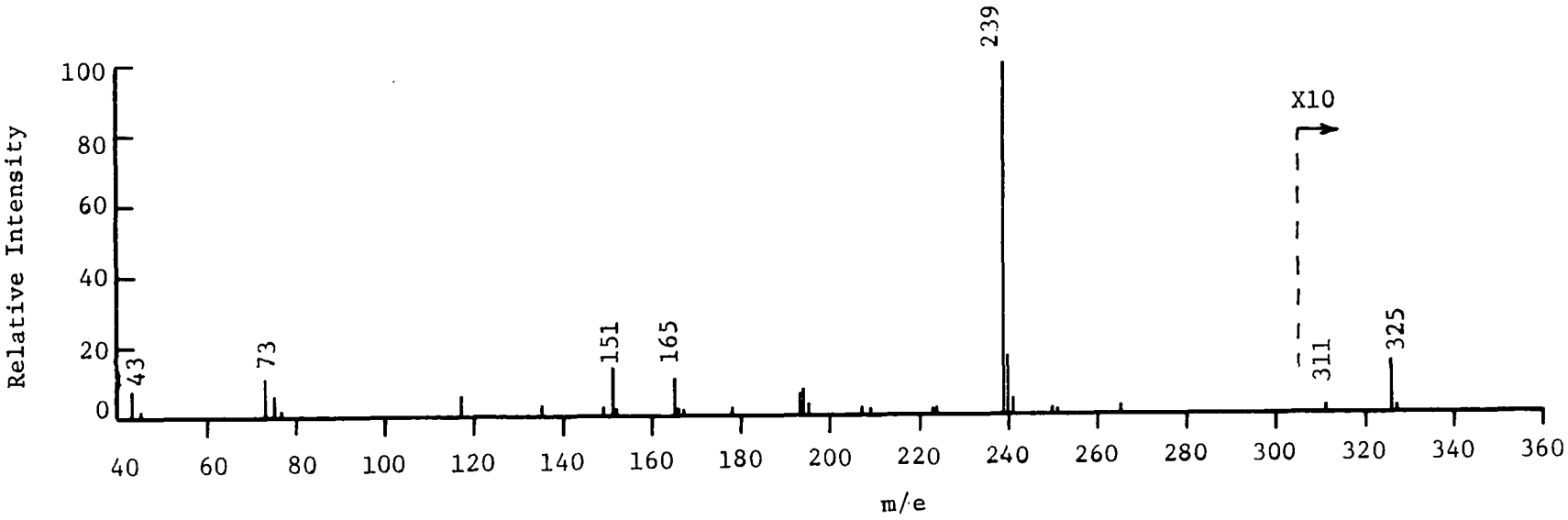
Figure 35. Mass Spectral Fragmentation Pattern and PMR Spectrum of the Trimethylsilyl Derivatives of Oxidation Products XLVIIIa and b

of the β-carbon proton but this is not as pronounced due to greater separation from the acetyl group than for the α-carbon proton. The fragmentation pattern shown in Fig. 35 also verifies this assignment. As was found for the bis-trimethylsilyl ether of diol XL, the major fragmentation leading to the base peak is due to α cleavage between the α- and β-carbon atoms in the side chain to give peaks at m/e 239 and m/e 117. In the case of oxidation products XLVIII, this cleavage gives the base peak at m/e 117 and the large peak at m/e 167. On the basis of this evidence it is concluded that these PA oxidation products are trimethylsilyl ethers of XLVIII. The isolation of two separate products having the same chemical formula is rationalized on the basis that these two products are the threo and erythro isomers as were found for diol XL.

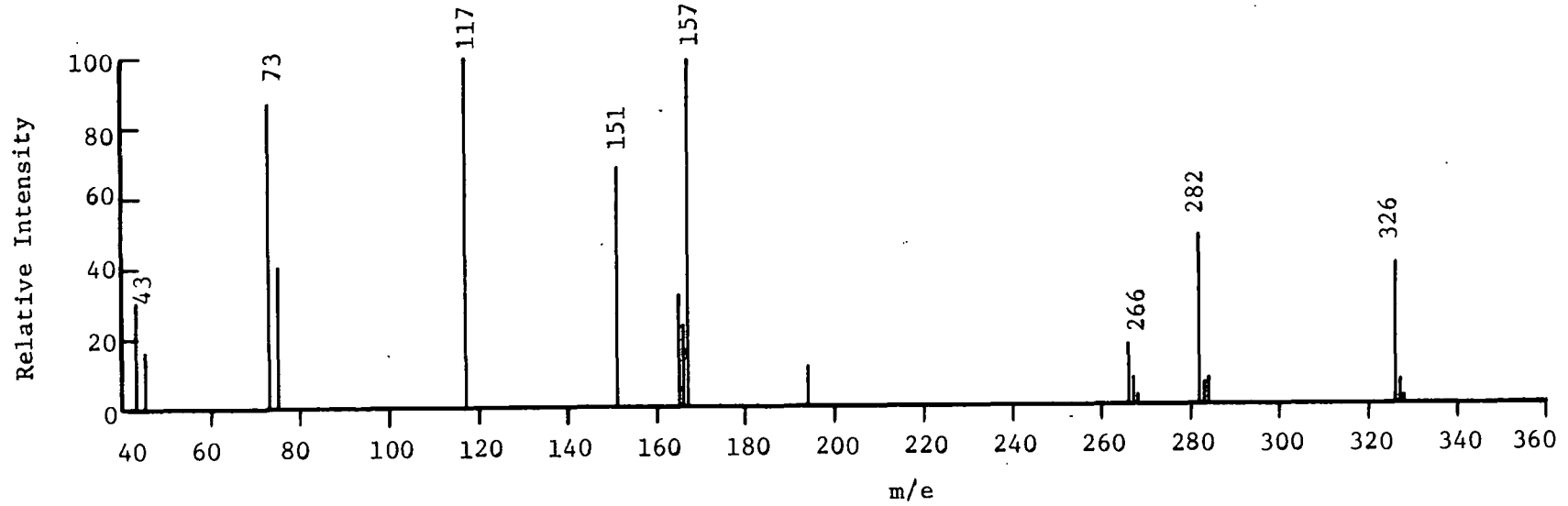
2-Acetoxy-1-(3,4-dimethoxyphenyl)propanol (XLIX)

The mass spectra of the trimethylsilyl derivatives of PA oxidation products XLVIII and XLIX are shown in Fig. 36. There are several peaks that both spectra have in common, m/e 43, 73, 151, and 165 in addition to the parent ion at m/e 326. The difference between these two spectra is due mostly to the base peak in XLIX at m/e 239 which is small in the mass spectra of XLVIIIa + b. Based on the structure assigned to XLVIII, it was expected that XLIX was the 2-O-acetyl derivative of diol XL.

The PMR data for the TMS derivative of XLIX are given in Fig. 37. The differences in the PMR spectra of XLIX and XLVIII can be explained by exchanging the position of the trimethylsilyl ether and the acetate ester. In XLIX, the acetate group is on the β-carbon of the side chain and causes a significant downfield shift for the proton on this carbon atom of 1.02 δ relative to the β-carbon atom on XLVIII, and 1.17 δ relative to the bis-TMS derivative of diol XL. The change in α-carbon atom substitution from acetoxy to trimethylsilyloxy in XLVIII and XLIX, respectively, is marked by a significant upfield shift of 0.99 δ for the



Mass spectrum of TMS ether of oxidation product XLIX

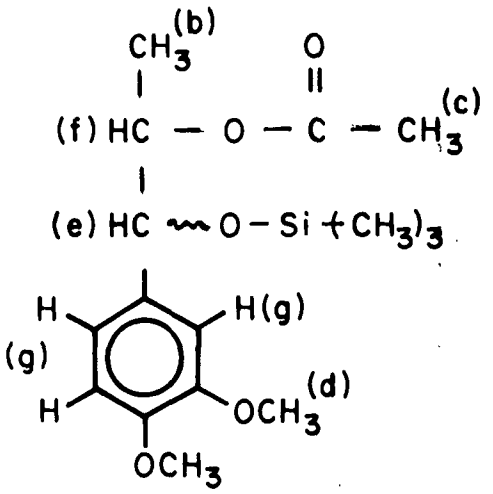


Mass spectrum of TMS ether of oxidation product XLVIIIa

Figure 36. Mass Spectra of TMS Ethers of Oxidation Products XLVIIIa and XLIX

Structure and PMR Spectrum

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
a)	0.03	Sing.	-	9
b)	1.01	Doub.	6	3
c)	2.03	Sing.	-	3
d)	3.87	Sing.	-	6
e)	4.51	Doub.	7	1
f)	5.02	Mult.	-	1
g)	6.7-6.9	Mult.	-	3



Mass Spectra Fragmentation Pattern

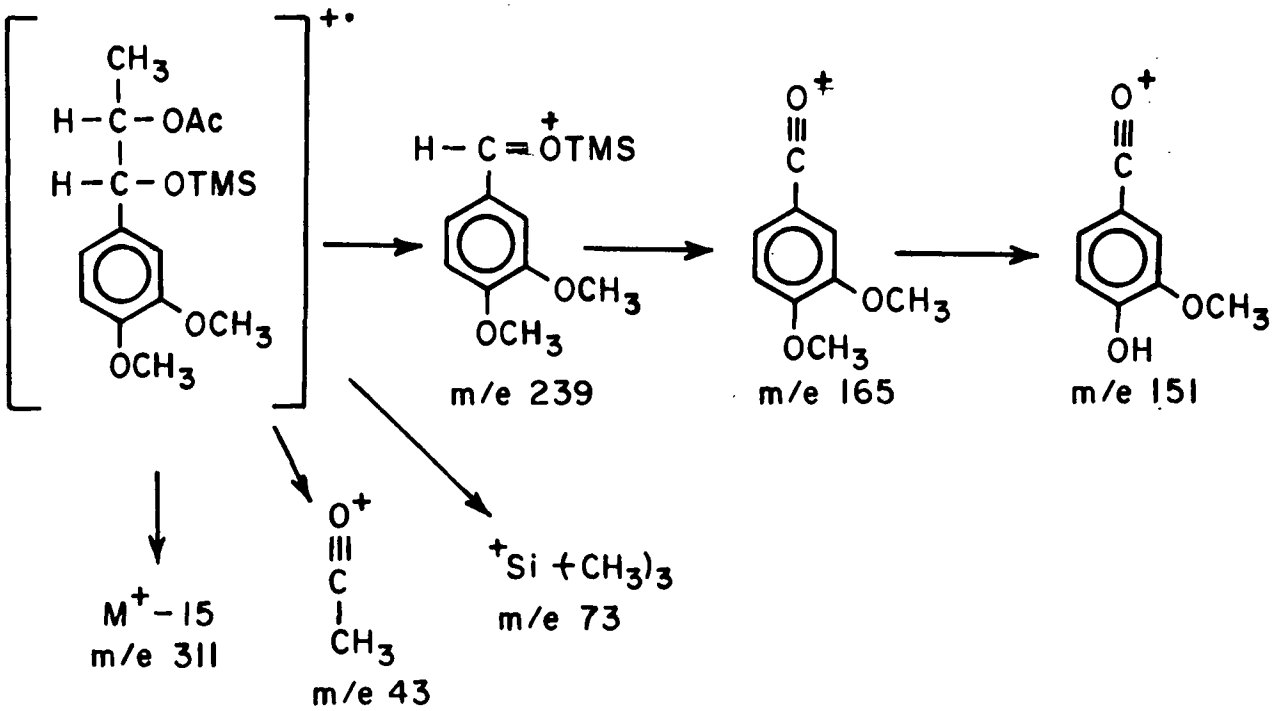


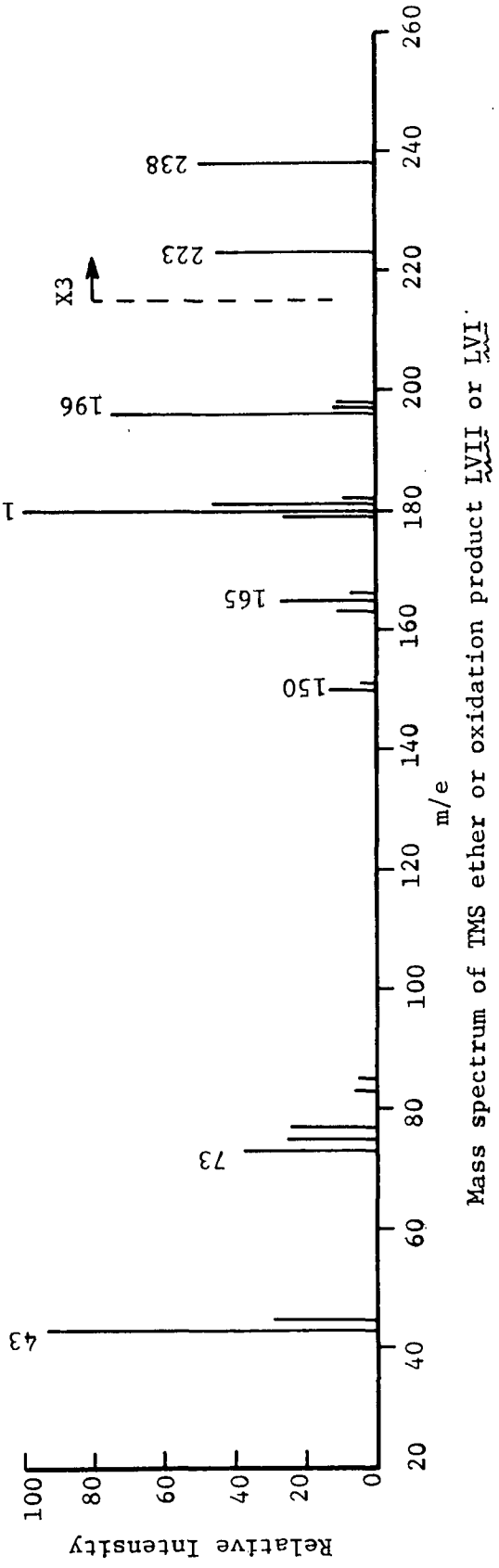
Figure 37. Mass Spectral Fragmentation Pattern and PMR Spectrum of the Trimethylsilyl Derivative of Oxidation Product XLIX

chemical shift of this proton. The signal for the proton on the α-carbon of the side chain is still shifted downfield by 0.21 δ in XLIX relative to the same proton in the bis-TMS ether of diol XL and this is again due to the acetoxy group at the β-carbon atom. The fragmentation pattern shown in Fig. 37 also shows the effect of the change in position of the acetoxy and trimethylsilyloxy groups in the side chain and accounts for the base peak at m/e 239 which was similarly the base peak in the bis-TMS ether of diol XL. Based on these observations it is concluded that the structure of PA oxidation product XLIX is 2-acetoxy-1-(3,4-dimethoxyphenyl)-propanol. The presence of only one product in this case does not eliminate the possibility of two diastereomers for this product as there were additional peaks in the gas chromatograph but these were not collected due to their small size.

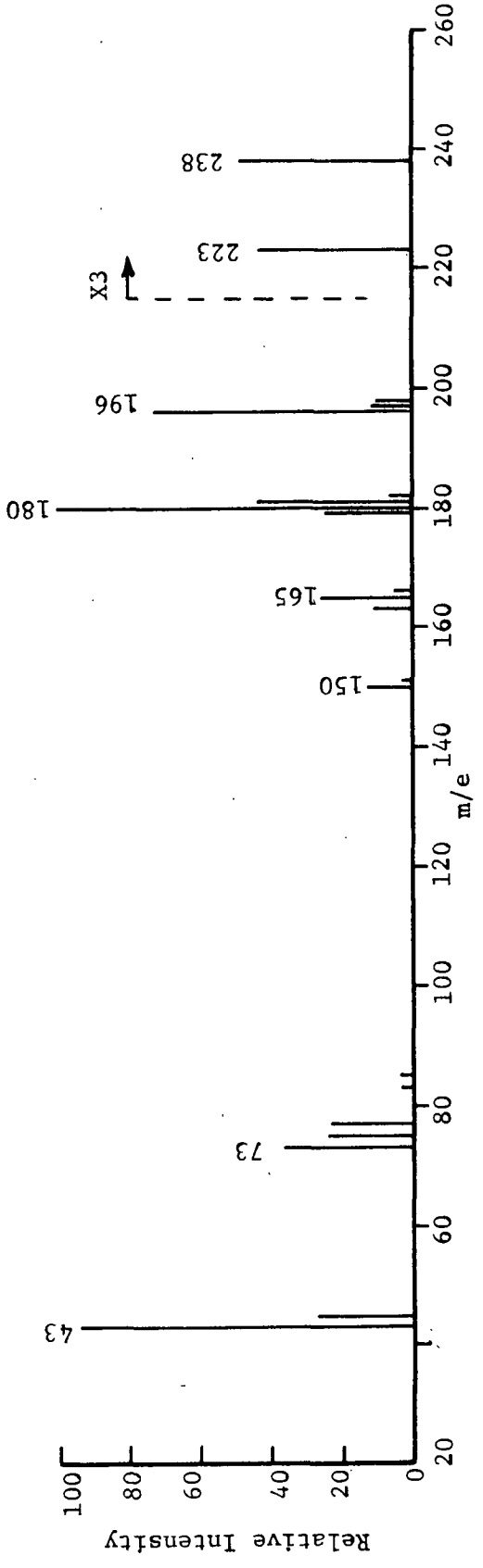
Monoacetyl-4-methylcatechols (LVI and LVII)

The mass spectra of the TMS derivatives of oxidation products LVI and LVII are shown in Fig. 38. The mass spectra are very similar even though they represent two overlapping but distinguishable peaks in the GLC. The PMR spectra are given in Fig. 39 and here again the match is nearly identical. The assignment of chemical shifts for the ring methyl versus the acetyl methyl groups was not possible. Values for the chemical shift of the ring methyl of the various products has a range of 2.27-2.31 δ and the range for aromatic acetoxy methyl chemical shifts was 2.26-2.30 δ.

The fragmentation patterns for these oxidation products are shown in Fig. 40. The presence of the acetyl group is indicated by the large peak at m/e 43 and the peak at m/e 196 (M-42) representing loss of ketene, a common fragmentation for aromatic acetates (47). A trimethylsilyl group is indicated by the large peak at m/e 73 and by the peak at m/e 223 (M-15). Similar to the TMS ether of creosol, the base peak comes at m/e 180, due to loss of the methoxy methyl and cyclization of the TMS function. The peak at m/e 181 is attributed to loss of silyl-methyl



Mass spectrum of TMS ether or oxidation product LVII or LVI



Mass spectrum of TMS ether of oxidation product LVI or LVII

Figure 38. Mass Spectra of TMS Ethers of Oxidation Products LVI and LVII

Structure and PMR Spectra

Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
Oxidation Product LVI			
a) 0.07	Sing.	-	9
b) 2.27	Sing.	-	3
c) 2.34	Sing.	-	3
d) 6.7-6.9	Mult.	-	3
Oxidation Product LVII			
a) 0.05	Sing.	-	9
b) 2.28	Sing.	-	3
c) 2.33	Sing.	-	3
d) 6.5-6.9	Mult.	-	3

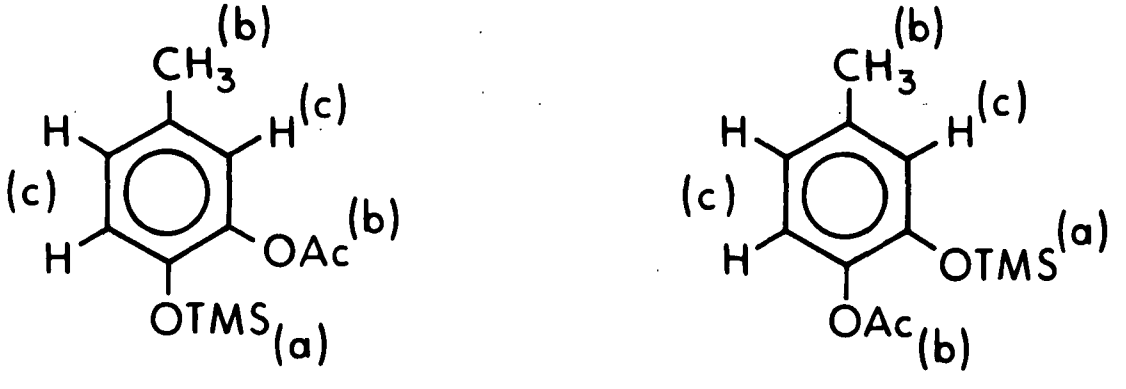


Figure 39. Structure and PMR Spectra of the Trimethylsilyl Derivative of Oxidation Products LVI and LVII

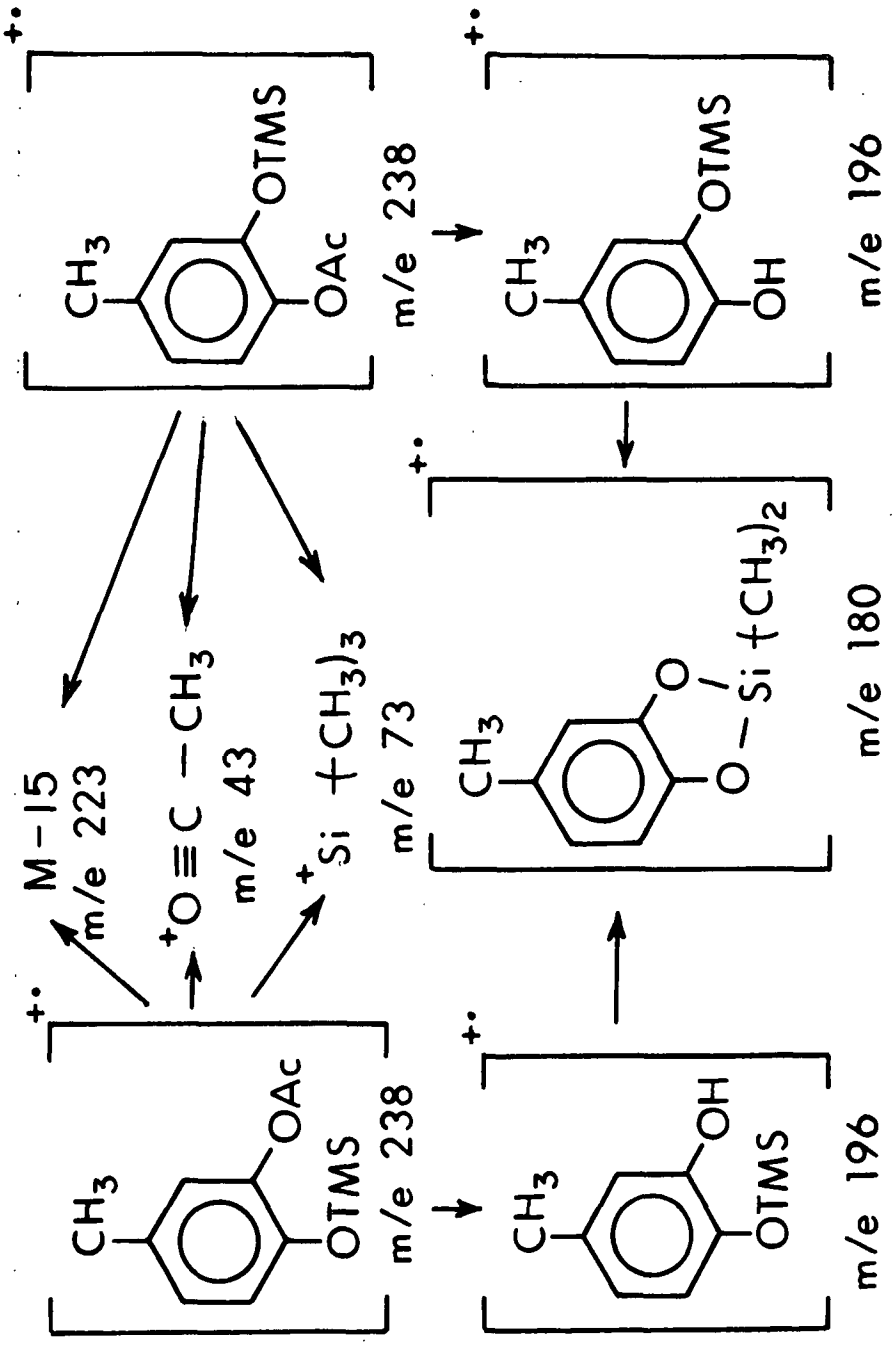


Figure 40. Mass Spectral Fragmentation Patterns for the Trimethylsilyl Derivative of Oxidation Products LVI and LVII

group from an uncharged 196 fragment as well as the ^{13}C isotope contribution from the ion at m/e 180.

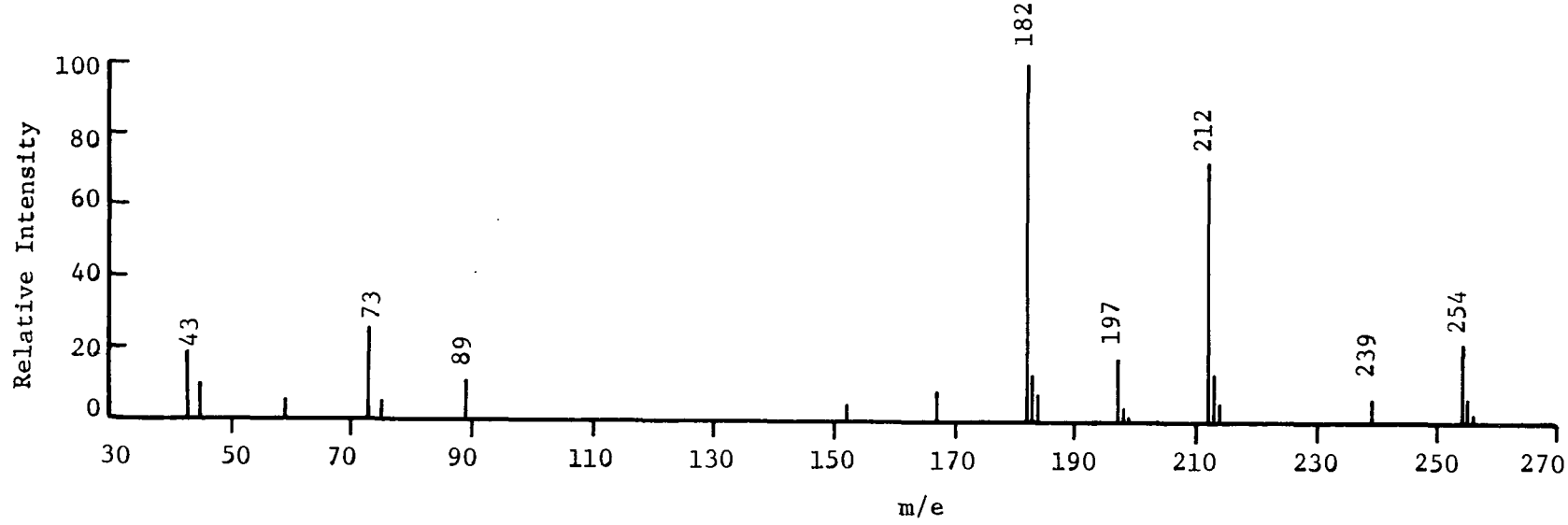
From this evidence it is concluded that oxidation products LV and LVI are 4-methylcatechol monoacetates. The fact that there were two separate peaks in the gas chromatogram shows that these products are not identical and are therefore the two isomeric monoacetates and 4-methylcatechol as shown in Fig. 38.

Methoxy-dihydroxyphenyl Acetates (LI and LIII)

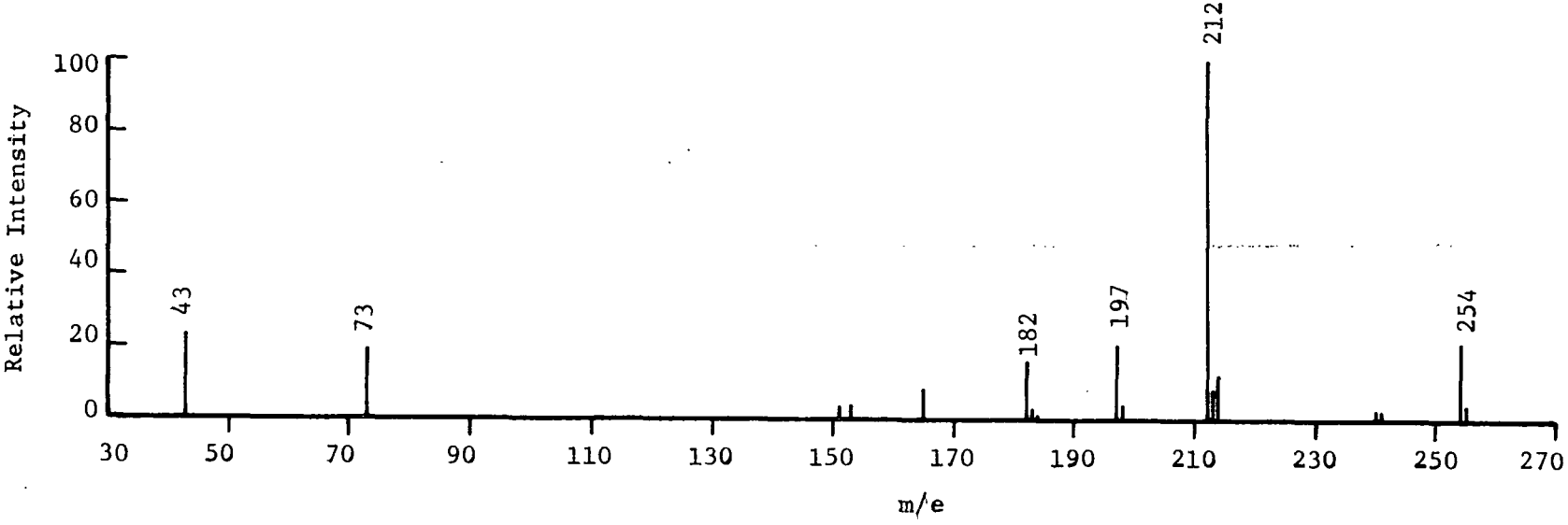
Two separate methoxydihydroxyphenyl acetates were isolated and characterized by PMR and mass spectrometry. The positions of the three oxy substituents are not known exactly, but their substitution pattern is that of 1,2,4-trihydroxybenzene. The origin of these products is the veratryl ring in β-ether XXXVI.

The mass spectra of the TMS ethers of PA oxidation products LI and LII are given in Fig. 41. Both products give the same parent ion at m/e 254. The fragment ions at M-15 (m/e 239) and m/e 73 indicate the presence of a trimethylsilyl group in the molecule. The peaks at m/e 43 and at M-42 (m/e 212) are characteristic of phenyl acetates (47).

The PMR spectra of the TMS ethers of LI and LIII are given in Fig. 42. These confirm the presence of the TMS and acetyl functions by the peaks in the 0.2 and 2.2 δ regions, respectively. The PMR spectra also indicate the presence of methoxyl and three aromatic protons by the signals at 3.7 and 6-7 δ regions, respectively. These functional groups then account for the total molecular weight as indicated by the mass spectra. Due to the structure of the starting material, the methoxy group is either in the 1 or 2 position. This leads to two sets of possible isomers, A + B and C + D as shown in Fig. 42.



Mass spectrum of TMS ether of oxidation product LII



Mass spectrum of TMS ether of oxidation product LI

Figure 41. Mass Spectra of TMS Ethers of Oxidation Products LI and LII

Structure and PMR Spectra

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
		Oxidation Product LI		
a)	0.26	Sing.	-	9
b)	2.28	Sing.	-	3
c)	3.77	Sing.	-	3
d)	6.3-6.9	Mult.	-	3
		Oxidation Product LII		
a)	0.23	Sing.	-	9
b)	2.26	Sing.	-	3
c)	3.78	Sing.	-	3
d)	6.3-6.9	Mult.	-	3

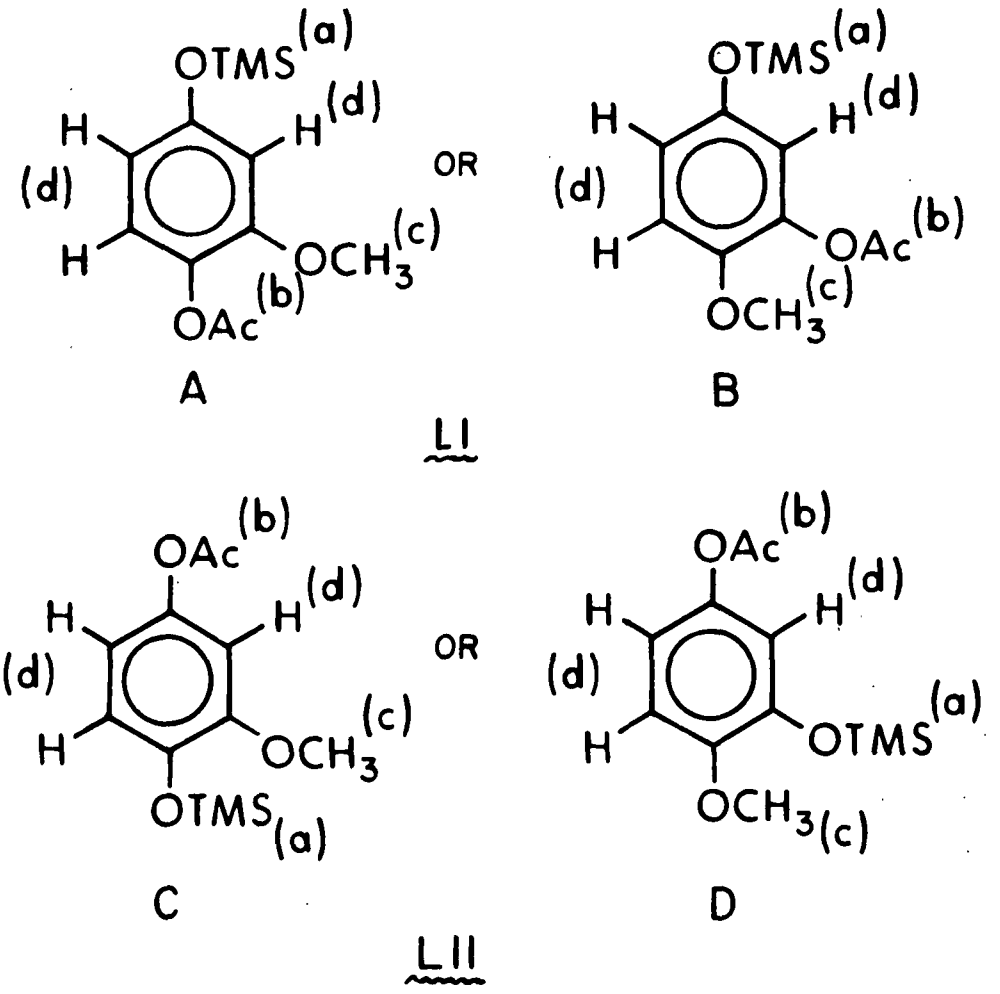
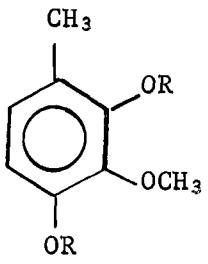


Figure 42. Structure and PMR Spectra of the Trimethylsilyl Derivatives of Oxidation Products LI and LII

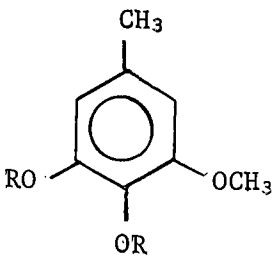
From the mass spectra it is possible to determine that one product is a 4-acetoxy and the other is a 4-trimethylsilyloxy substituted product. The main difference in the mass spectra is the large peak at m/e 182 which is the base peak in LI and is absent in LII. Based on the fragmentation pattern of the TMS ethers of oxidation products LIV, LV and LVI, the base peak for LI is due to the formation of the cyclic dimethylsilyldioxy fragment ion shown in Fig. 43 at m/e 182. On this basis, the structure of LI is assigned either structure A or B as shown in Fig. 42. The absence of this peak at m/e 182 is concluded to indicate that the trimethylsilyloxy group in LII is not ortho to the methoxyl group and therefore has structure C or D as shown in Fig. 42.

5-Acetoxy Substituted Creosol and Creosol Acetate (LVIII and LIX)

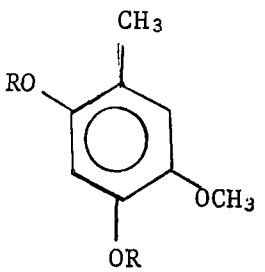
Two oxidation products were isolated as trimethylsilyl and acetyl derivatives of 5-acetoxy substituted 2-methoxy-4-methylphenols as indicated by their PMR and mass spectra. The PMR spectrum and mass fragmentation pattern for LVIII and LIX are given in Fig. 44 and 45, respectively. In both cases the signal for the aromatic protons were a pair of singlets. Of the three possibilities for these products as shown below, this pattern for the aromatic protons eliminates structure A.



A



B



C

If the product were A, the two remaining aromatic protons would be ortho and would show some coupling in the PMR spectra (46). This assignment also agrees with the results of Farrand (19) which showed no substitution in this position in

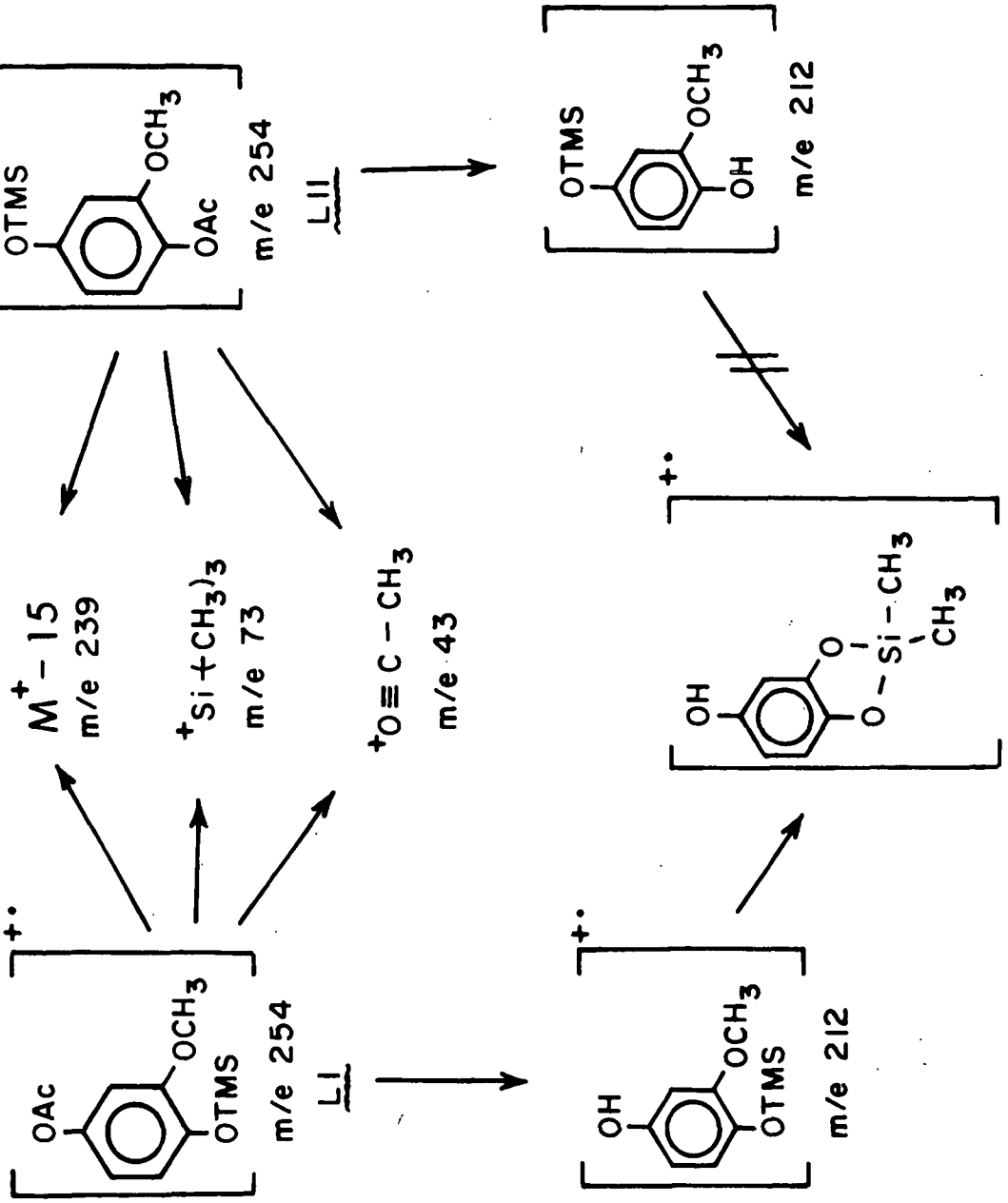
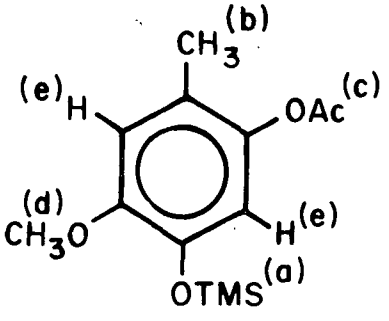


Figure 43. Mass Spectral Fragmentation Pattern for the Trimethylsilyl Derivative of Oxidation Products LI and LII

PMR Spectrum of TMS Ether of LVIII

Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
a) 0.22	Sing.	-	9
b) 2.09	Sing.	-	3
c) 2.27	Sing.	-	3
d) 3.78	Sing.	-	3
e) 6.59,6.67	Pr. sing.	-	2



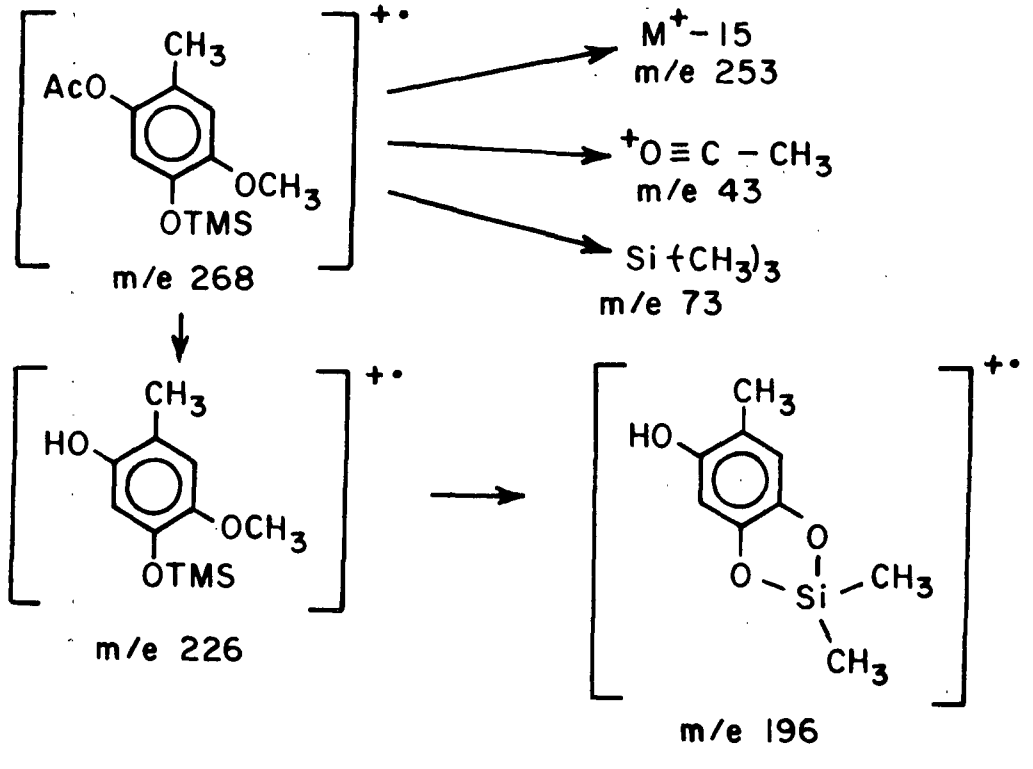


Figure 44. Mass Spectral Fragmentation Pattern and PMR Spectrum of the Trimethylsilyl Derivative of Oxidation Product LVIII

PMR Spectrum of Oxidation Product LIX

Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
a) 2.16	Sing.	-	3
b) 2.29	Sing.	-	6
c) 3.80	Sing.	-	3
d) 6.77,6.79	Pr. sing.	-	2

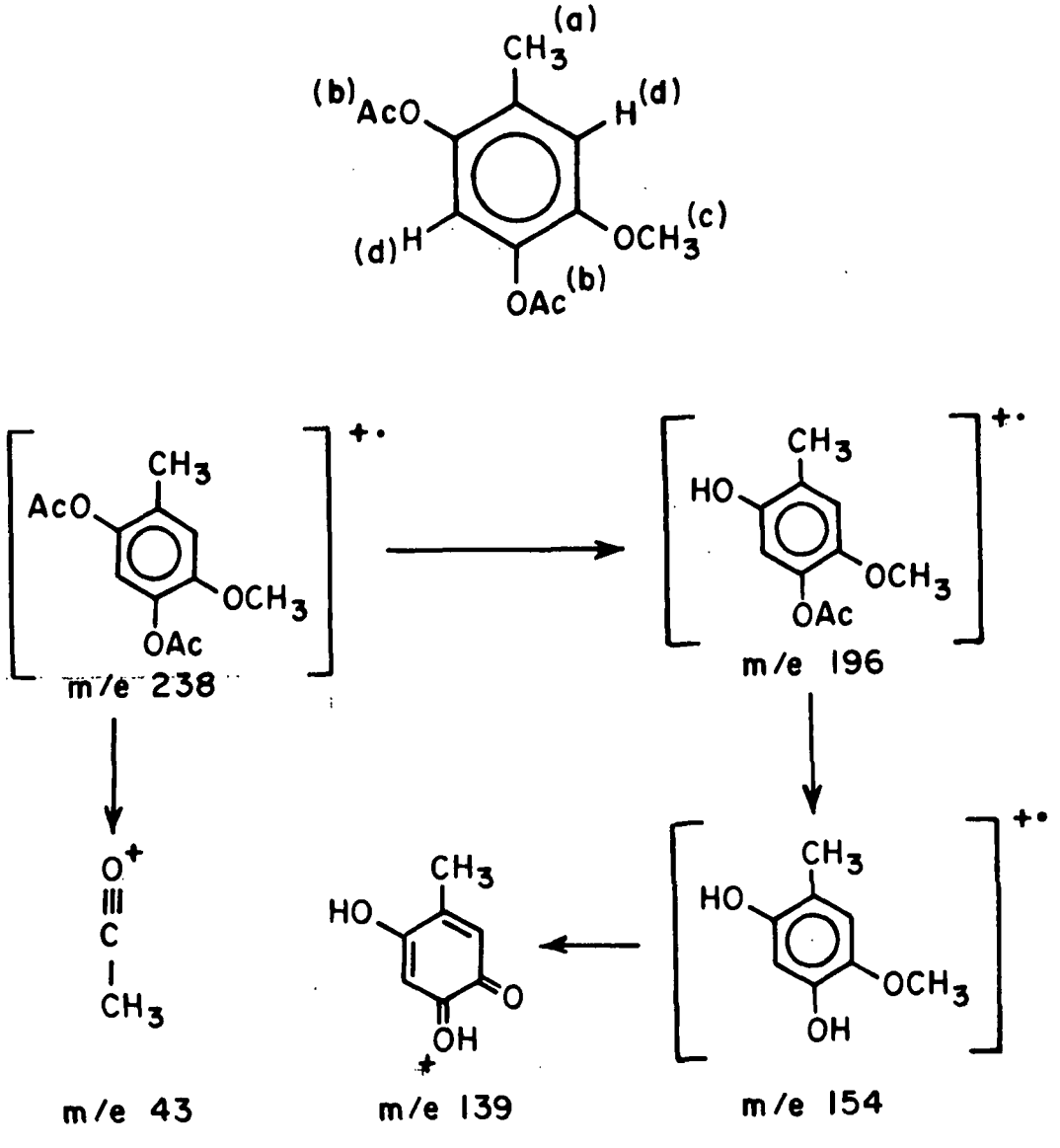


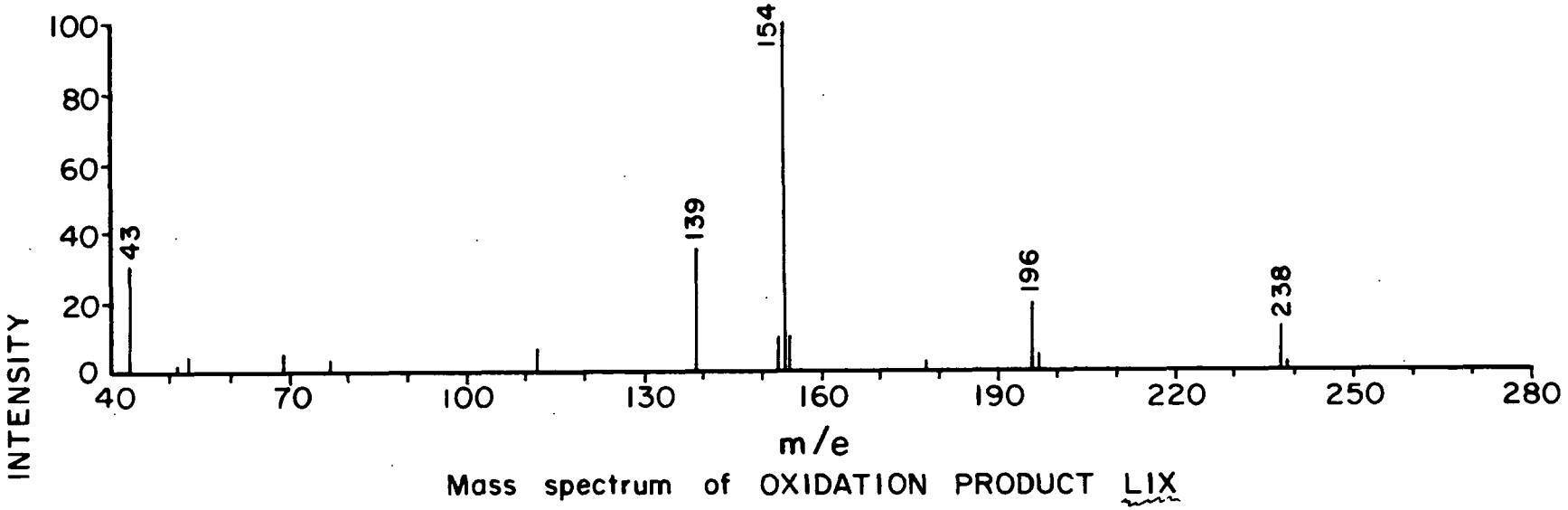
Figure 45. Mass Spectral Fragmentation Pattern and PMR Spectrum of Oxidation Product LIX

the PA oxidation of dioxy substituted aromatic ring systems. The most favored isomer is C which indicates para positioning of the aromatic protons. The upfield shift of the ring methyl protons' signal in LI and LII is due to the presence of the acetoxy group ortho to the ring methyl group. Similar shifts have been reported for related compounds having an acetoxy group ortho to a ring methyl group (48,49). In particular, it was found that the ring methyl proton signal for o-, m- and p-cresol acetates were 2.13, 2.33 and 2.30 δ, respectively (48). This shift is due to a shielding zone associated with the carbonyl function in the acetoxy substituent (46). In addition, para protons do not normally show coupling (46), and the aromatic proton signals would be singlets as was found experimentally for LVIII and LIX. It is concluded therefore that the additional oxygen-substituent on the creosol ring of LVIII and LIX is in the 5 position.

It is also of interest to note the fragmentation pattern of LVIII as seen in Fig. 44. One of the three major peaks in the mass spectrum is that at m/e 196 arising from the same cyclic dimethylsilyldioxy structure as found for other ortho oxy substituted trimethylsilyl ethers. The small peak at m/e 238 may also be accounted for by a structure of this type but it would be expected to be small due to the ease of fragmentation of the acetyl group. The assignment of the structure for m/e 196 also defines the position of the free hydroxyl group in the underivatized oxidation product. The mass spectra of these two products are given in Fig. 46.

ARYLPROPYL-β-ARYL ETHER TYPE OXIDATION PRODUCTS

There were several PA oxidation products of very low yields that were not eluted from the GLC column except at higher temperatures (>220°C) and whose retention times were greater than that of the TMS ether of the starting material.



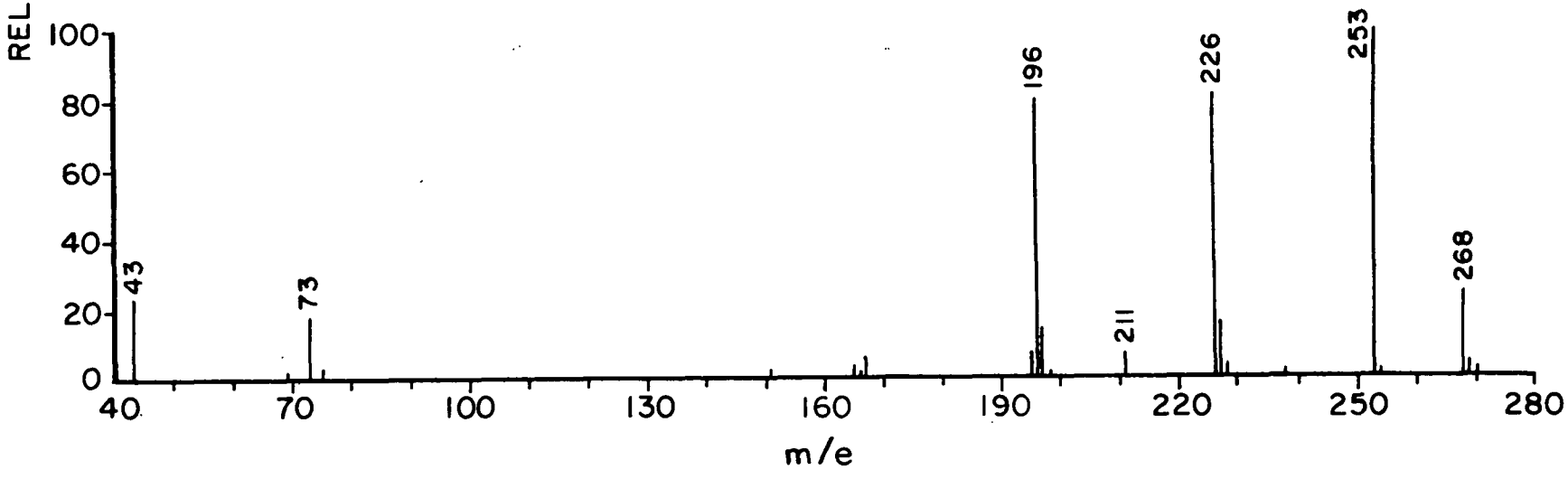


Figure 46. Mass Spectra of Oxidation Product LIX and TMS Ether of Oxidation LVIII

This suggested that these products could be structurally related to the starting material and their structures would provide useful information about the PA oxidation of β-ether XXXVI. The exact structure of only one of these compounds could be determined and this was for XXXVII as previously described. Without an extensive collection of known compounds to accurately define the subtle variations in the PMR and mass spectral data, it was not possible to deduce the exact structures of the remaining products of this type. It was possible to show that the β-aryl ether bond remained intact and these oxidation products were the result of ring hydroxylation and demethylation.

Perhaps the most interesting of these products is oxidation product LXIII. The PMR spectrum and a possible structure for the TMS ether of LXIII are given in Fig. 47. The PMR data show a TMS group (s, 0.09 δ), γ-methyl group (d, 1.00 δ), two methoxyl groups (s, 3.86 δ and 3.88 δ), β-CH (m, 3.95 δ) and α-CH (d, 5.51 δ). From the position of the α-CH proton chemical shift, which is downfield 0.7 δ from that of the TMS ether of XXXVI, it is concluded that there is an acetate ester at this position and this is the singlet at 2.08 δ. The aromatic proton singlet at 6.83 δ indicates that there are three very similar aromatic protons and that these are not ortho substituted. The signal at 2.16 δ is due to the aromatic methyl and aromatic acetoxy protons. The integral of this peak indicates 3 or 4 aromatic acetoxy groups. Based on the other substituents, there are three aromatic acetoxy groups. There are many possible structures and one such possibility is shown in Fig. 47. The mass spectrum of the TMS ether of LXIII is given in Fig. 48. Several possible structures are proposed for the fragment ions found in the mass spectrum of LXIII and these are shown in Fig. 49.

The PMR spectrum and structure for the TMS derivative of oxidation product LXII are given in Fig. 50. The PMR spectrum indicates an aliphatic and an aromatic trimethylsilyl ether by the signals at 0.07 and 0.25 δ, respectively.

Structure and PMR Spectrum of Oxidation Product LXIII

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
a)	0.08	Sing.	-	9
b)	1.00	Doub.	6	3
c)	2.08	Sing.	-	3
d)	2.16	Sing.	-	14
e)	3.86,3.88	Sing.	-	6
f)	3.95	Mult.	-	1
g)	5.51	Doub.	6	1
h)	6.83	Sing.	-	3

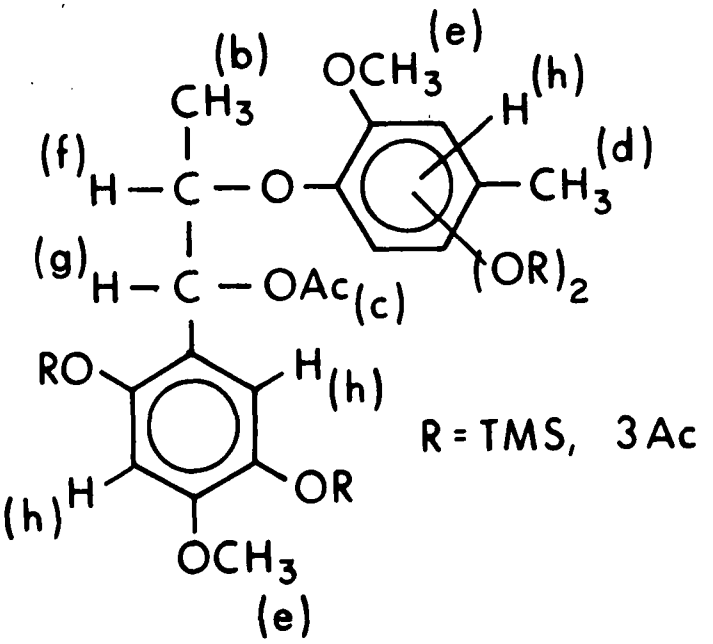
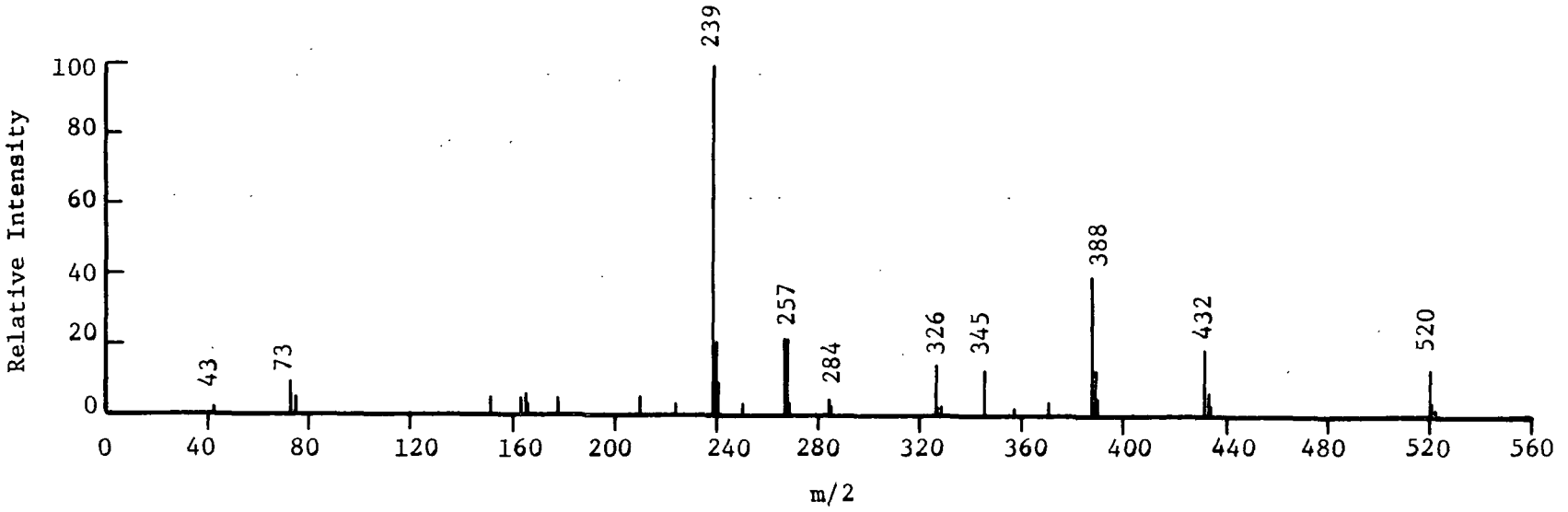
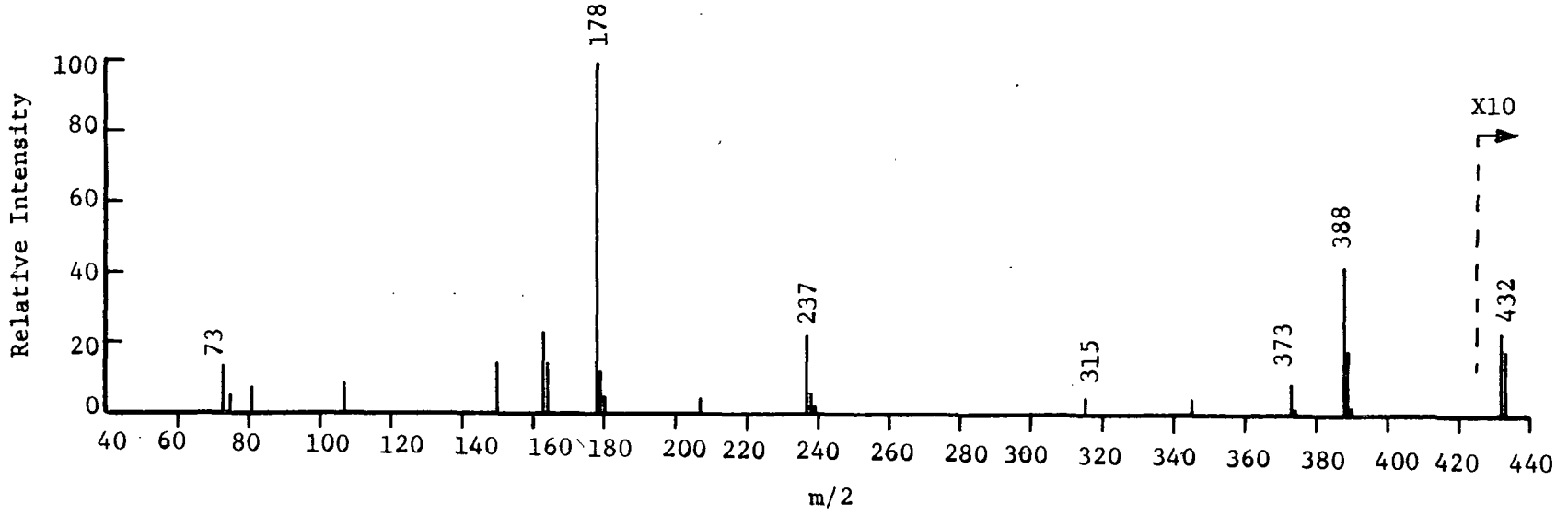


Figure 47. PMR Spectral Data and Possible Structure for the Trimethylsilyl Derivative of Oxidation Product LXIII

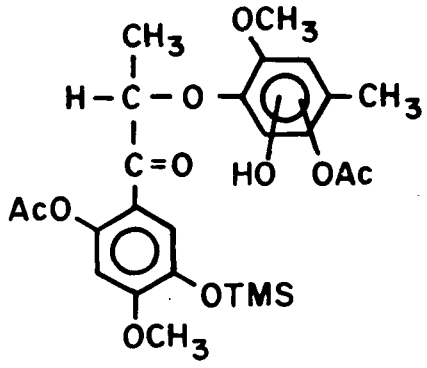


Mass spectrum of TMS ether of oxidation product LXIII

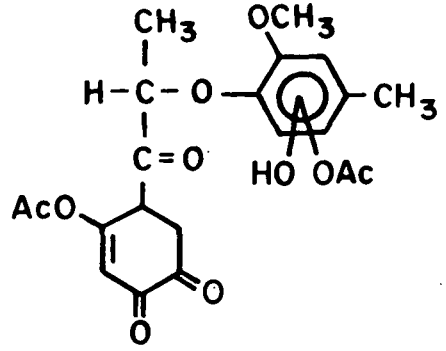


Mass spectrum of TMS ether of oxidation product LXII

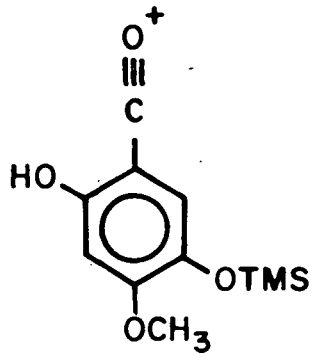
Figure 48. Mass Spectra of TMS Ethers of Oxidation Products LXII and LXIII



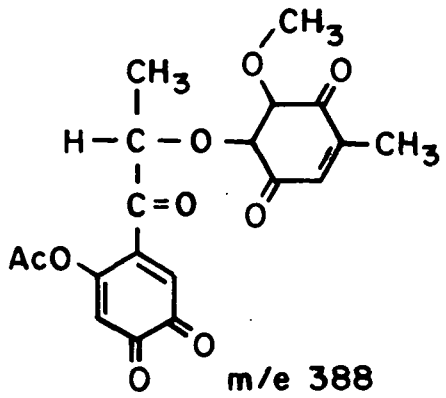
m/e 520



m/e 432



m/e 239



m/e 388

Figure 49. Possible Fragment Ions for TMS Ether of Oxidation Product LXIII

Possible Structure and PMR Spectrum of Oxidation Product LXII

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
a)	0.07	Sing.	-	7
b)	0.25	Sing.	-	9
c)	1.14	Doub.	6	3
d)	2.09	Sing.	-	3
e)	3.89	Sing.	-	6
f)	4.08	Mult.	-	1
g)	4.52	Doub.	8	1
h)	6.4-6.9	Mult.	-	6

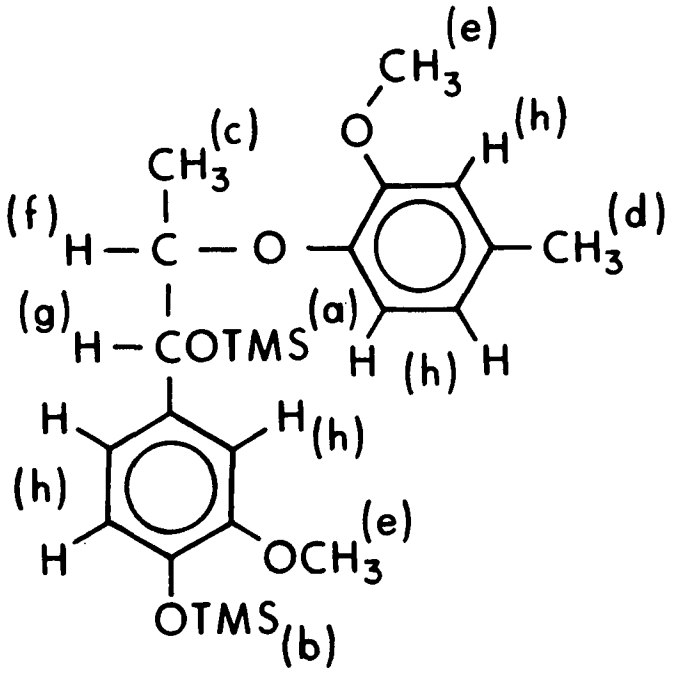
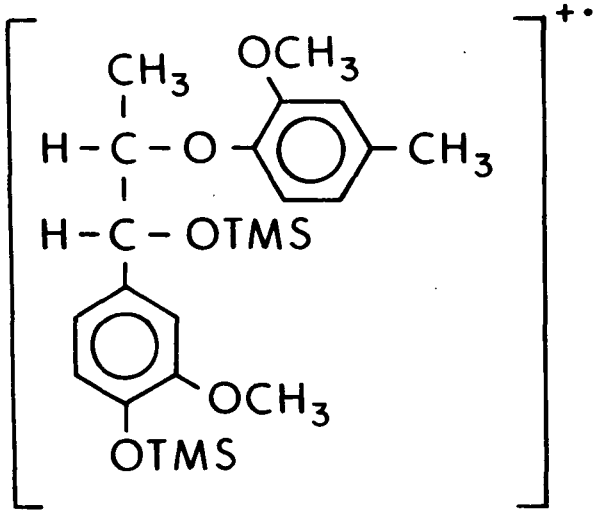
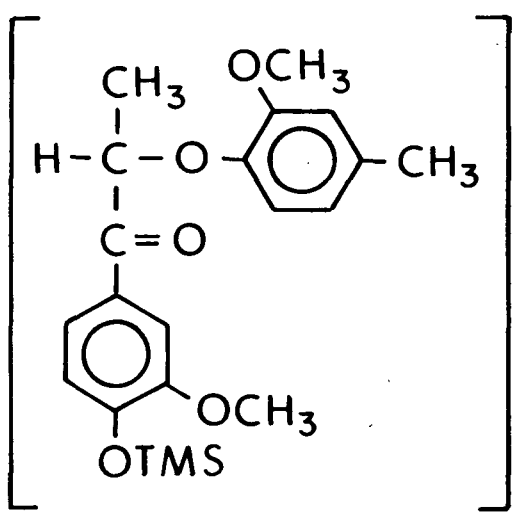


Figure 50. PMR Spectrum and Possible Structure for the Trimethylsilyl Derivative of Oxidation Product LXII

In comparison to LXIII, the signal for the proton on the α-carbon atom is shifted upfield to 4.52 δ, a value that compares favorably with that for the TMS ether of β-ether XXXVI, at 4.75 δ. The PMR spectrum also indicates the presence of two methoxyl groups, an aromatic ring methyl group and the γ-methyl group of the side chain at 3.89, 2.09, and 1.14 δ, respectively. The PMR evidence indicates therefore that product LXII is the result of demethoxylation of one methoxyl group from XXXVI by PA. The demethoxylation is proposed to occur in the veratryl ring due to the changes in the mass spectrum between the TMS ethers of LXII and XXXVI. With no change in the veratryl ring a peak would be expected at m/e 239. This peak appears from the data found in this study to be diagnostic for the trimethylsilyl ether of α-substituted veratryl alcohol structures, and is absent in LXII. The mass spectrum of LXII is given in Fig. 48, and several possible fragment ions are proposed in Fig. 51. The origin of the base peak at m/e 178 is unknown. It is interesting to note that a fragment of the same mass to charge ratio is found in both XXXVII and the TMS ether of XXXVI, although the mass spectral peak for these is of much lower intensity.



m/e 462 (absent)



m/e 388

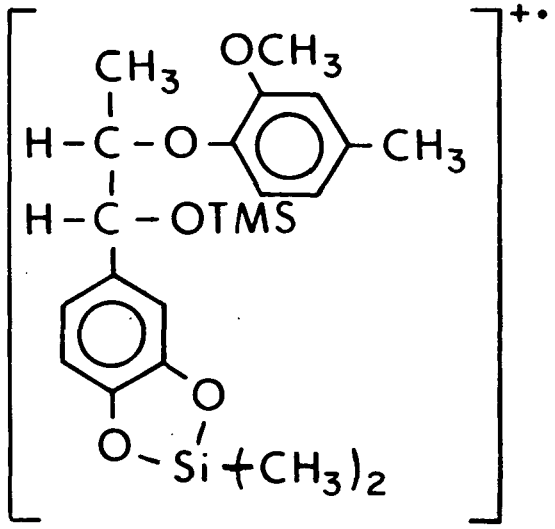


Figure 51. Possible Fragment Ions for TMS Ether of Oxidation Product LXII

CONCLUSIONS

Identification of the principal peroxyacetic acid oxidation products of the lignin-related model compound, 1-(3,4-dimethoxyphenyl)-2-(2-methoxy-4-methylphenoxy)propanol XXXVI, shows that there are at least five major types of initial oxidation.

The presence of several veratryl type oxidation products shows that cleavage of the methoxyl groups in the veratryl ring is not necessary for cleavage of the interaryl linkage as had been previously claimed. This finding is significant in the extrapolation of model compound peroxyacetic acid reactions to those expected with lignin. The previously reported results suggested that β-aryl ether cleavage in the lignin macromolecular structure would occur only in those arylpropyl-β-aryl ether structures where there was at least one free hydroxyl in the arylpropyl aromatic ring. The findings of this study show that such a free hydroxyl group is not required for peroxyacetic acid oxidative cleavage of arylpropyl-β-aryl ether structures.

Three different products resulting from the peroxyacetic acid oxidation of a β-aryl ether compound, 4-methylphenol, 2-keto-arylpropyl and 2-hydroxy-arylpropyl products, were found. These products were the result of β-ether bond cleavage by peroxyacetic acid. Since it was determined that hydrolytic cleavage under the temperature and reaction solvent conditions used for the oxidation could not account for these products, it is concluded that there are two distinct routes involved in peroxyacetic acid β-aryl ether bond cleavage. The first route leads to the 4-methylphenolic and 2-keto-arylpropyl products and the second leads to the 2-hydroxy-arylpropyl product and an o-benzoquinone product which was not isolated due to its high reactivity with peroxyacetic acid. Possible mechanisms for these reactions have been proposed.

Isolation of 2-keto-β-aryl ether and 2-aryloxypropionaldehyde peroxyacetic acid oxidation products shows there are at least two routes involved in cleavage about the α-carbon atom of a β-aryl ether structure. The 2-keto-β-aryl ether product results from oxidation of the benzylic hydroxyl group to a carbonyl and is subsequently oxidized by Baeyer-Villiger reactions to give cleavage products. The 2-aryloxypropionaldehyde product is the result of side-chain displacement by an electrophilic aromatic substitution reaction of peroxyacetic acid with the β-aryl ether compound.

A fifth type of primary reaction of β-aryl ether compounds with peroxyacetic acid involves ring hydroxylation and/or demethoxylation and shows the effectiveness of this reagent for electrophilic substitutions. Although this type of reaction may not result directly in cleavage of the interaryl linkage, it does activate the substrate toward further oxidation as evidenced by the low yields of these products. The isolation of several "monomeric" products from these reactions strongly suggests the importance of secondary reactions of this type.

Isolation of muconic acid type products supports previous evidence for aromatic ring cleavage by peroxyacetic acid. The identification of 5-carboxymethyl-4-methyl-2(5H)furanone as an oxidation product suggests that oxidation of o-oxy-substituted aromatic systems by peroxyacetic acid to muconic acids may occur without prior formation of o-benzoquinones.

EXPERIMENTAL PROCEDURES

GENERAL ANALYTICAL PROCEDURES

MELTING POINTS

Melting points were taken on a Thomas-Hoover capillary melting point apparatus that had been calibrated using a variety of known samples.

MEASUREMENT OF pH

All pH measurements were made with a Beckman Model 96 pH meter equipped with Corning pH electrode and Corning reference electrode (calomel electrode). Standardization of the electrodes was done with BuffAR (Mallinckrodt) standard buffer solutions of pH 4.01, 7.00, and 9.00.

INFRARED SPECTROPHOTOMETRY

All infrared spectra were run on a Perkin-Elmer Model 700 recording spectrophotometer.

PROTON MAGNETIC RESONANCE SPECTROMETRY

PMR spectral analyses were done with a Varian A-60A spectrometer (60 MHz spectra) and a Jeol FX100 FT-NMR spectrometer (100 MHz spectra). Solvents used were Silanor C (99.8% $CDCl_3$ containing 1% (v/v) tetramethylsilane) (Merck, Sharp and Dohme), Silanor DMSO (99.5% d_6 DMSO containing 1% tetramethylsilane) and 99.8% $CDCl_3$ (Aldrich and Bio-Rad). The internal standards used were the tetramethylsilane signal at 0.00 δ and the $CHCl_3$ signal at 7.24 δ. It was necessary to use the chloroform signal in analysis of the trimethylsilyl derivatives as the tetramethylsilane signal would interfere with peak assignment and integration in these cases.

CHROMATOGRAPHY

THIN-LAYER AND COLUMN CHROMATOGRAPHY

Thin-layer chromatography was done using microscope slides coated with silica gel G (Brinkman Inst.). The slides were developed by spraying with 20% (v/v) sulfuric acid in methanol and heating on a hot plate. Carbonyl compounds were detected using a 2,4-dinitrophenylhydrazine spray reagent prepared according to Swinehart (50). Column chromatography was done using 60-200 mesh chromatographic grade silica gel (Sargent-Welsh).

PREPARATIVE GAS CHROMATOGRAPHY

Preparative gas chromatography was done using a Varian Aerograph 200 gas chromatograph with a thermal conductivity detector. A detector current of 100 ma was used. Prepurified helium (Matheson Gas Products) was used as the carrier gas at a rate of 30 mL/min. Columns used were a 5 ft and a 10 ft x 1/4 inch stainless steel column packed with 5% OV-17 on 80/90 Anakrom ABS. Samples were collected in glass collectors shown in Fig. 52. The collectors were sealed with Parafilm M (American Can Co.) between injections and stored in a desiccator over P_2O_5 until PMR analyses could be made. Samples were then transferred to the PMR tubes by several rinses with the appropriate deuterated solvent.

GAS CHROMATOGRAPHY

Quantitative and qualitative gas chromatography studies were done on a Varian Aerograph 1200 gas chromatograph equipped with a hydrogen flame ionization detector and a Honeywell Electronic 16 recorder equipped with a Disc integrator. Prepurified nitrogen (Matheson Gas Products) was used as the carrier gas. The following variables were used for the various analyses:

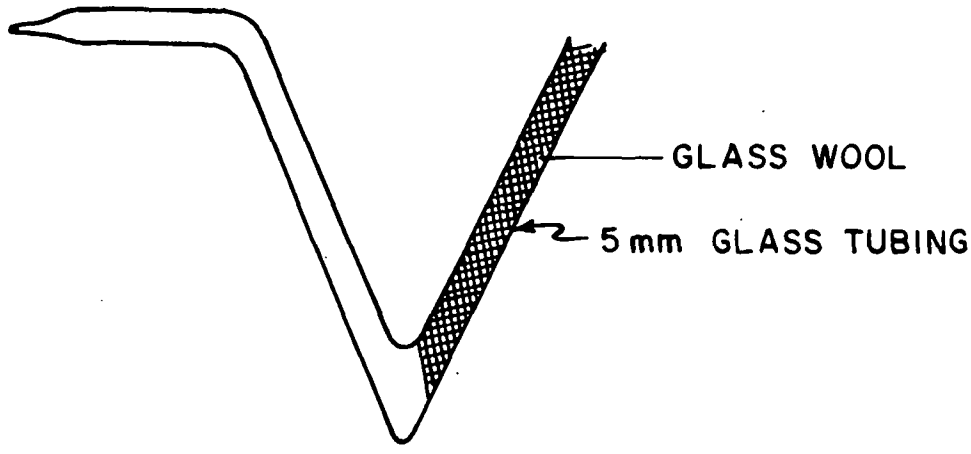


Figure 52. Collectors Used in Preparative Gas Chromatography

Analysis of β-ether XXXVI

Internal standard: 4'-benzyloxy-3'-methoxypropiophenone

Column: 4' x 1/8" stainless steel column equipped for on-column injection packed with 5% SE-30 on 60/80 mesh AW/DMCS treated Chromosorb W

Flow rate: 30 mL/min

Oven temperature: 230°C, isothermal

Injector temperature: 270°C

Detector temperature: 270°C

Analysis of diol XL and ketol XLI

Internal standard: 1-(3,4-dimethoxyphenyl)ethanol

Column: 10' x 1/8" stainless steel column equipped for on-column injection packed with 10% SE-30 on 90/100 mesh Anakrom SD

Flow rate: 30 mL/min

Oven temperature: 130°C for 6 min, then 2°/min to 170°C

Injector temperature: 220°C

Detector temperature: 250°C

Analysis of neutral and phenolic oxidation products of XXXVI

Internal standard: 1-(3,4-dimethoxyphenyl)ethanol

Column: 5' x 1/8" stainless steel column equipped for on-column injection packed with 5% OV-17 on 80/90 mesh Anakrom ABS

Flow rate: 20 mL/min

Oven temperature: 100°C hold for 6 min, then 2°/min to 230°C

Injector temperature: 270°C

Detector temperature: 300°C

Analysis of acidic oxidation products of XXXVI

Internal standard: hexadiendioic acid

All other variables were the same as for neutral and phenolic oxidation product analysis

GAS CHROMATOGRAPHY-MASS SPECTROMETRY

Mass spectral analyses were done on a Du Pont 21-491 mass spectrometer interfaced via a jet separator with a Varian Aerograph 1400 gas chromatograph equipped with a hydrogen flame ionization detector. Mass spectra were recorded with a Century GPO 460 oscillographic recorder. Helium (UHP helium, minimum purity 99.999%, Matheson Gas Products) was used as the carrier gas. Perfluorokerosene, low-boiling (PCR, Inc.) was used as a mass standard by continuous bleed on separate scans to the source area for assignment of mass to charge values for all samples. Other variables were as follows:

GLC block temperature: 300-310°C

GLC to MS inlet tube temperature: 300-310°C

Source temperature: 150-220°C

Filament: GC, this results in a current of 50 ma and 75 v when scanning and 20 v when not scanning

Scan rate: 10 and 15 sec/decade

Pressure: 1-3 x 10^{-7} torr

Chart speed: 4 inches/sec

Filter frequency: 100 Hz

GLC column: 5' and 15' x 1/8" stainless steel columns equipped for on-column injection and packed with 3% OV-17 on 80/100 mesh Supelcoport

PREPARATION OF COMPOUNDS

COMMERCIAL AND DONATED CHEMICALS

Guaiacol and creosol were obtained from Eastman Organic Chemicals. Benzyl bromide, propionyl chloride, acetovanillone, ethyl 2-bromopropionate and 1-(3,4-dimethoxyphenyl)propan-2-one were obtained from Aldrich Chemical Co. Vanillin and 3',4'-dihydroxypropiophenone were obtained from K&K Laboratories, Inc. Tri-Sil concentrate and N,O-bis-trimethylsilyltrifluoroacetamide (BSTFA) were obtained from Pierce Chemical Co. Samples of veratraldehyde, hexadienedioic acid and veratric acid were obtained from the personal collection of Dr. I. A. Pearl. Samples of cis,trans-3-methylmuconic acid and 5-carboxymethyl-4-methyl-2(5H)-furanone were obtained from Dr. D. C. Johnson.

SOLVENTS

Anhydrous methanol (51), pyridine (52), chloroform (53), and dichloromethane (52) were purified using standard procedures. Anhydrous chloroform used in the preparation of trimethylsilyl derivatives for GLC analyses was stored in sealed vials equipped with septum tops. Silylation grade N,N-dimethylformamide was purchased from Pierce Chemical Co.

SYNTHESIS OF COMPOUNDS

The following compounds were prepared as previously described in the literature: methoxyhydroquinone (54), methoxyquinone (55), 3,4-dimethoxyphenol (56), 1-(3,4-dimethoxyphenyl)-1-hydroxypropan-2-one (57), 2-bromopropioveratrone (58), propiovanillone (59), 1-(3,4-dimethoxyphenyl)propan-1,2-diol (58), and 1-(3,4-dimethoxyphenyl)ethanol (60). The physical constants of these compounds were in good accord with the values reported in the literature. In addition, proton magnetic resonance, mass spectrometry and infrared spectrophotometry supported the structures in all cases.

Acetylation

The following procedure was used to prepare acetylated derivatives of methoxyhydroquinone, 3,4-dimethoxyphenol, 1-(3,4-dimethoxyphenyl)propan-1,2-diol and creosol. Ten to thirty milligrams of compound to be acetylated was placed in a 10-mL Erlenmeyer flask and shaken overnight with 1.5 mL of acetic anhydride and 6 mL of pyridine. The solution was then poured into 30 mL of chloroform and extracted with 1N hydrochloric acid (3 x 50 mL) and distilled water (3 x 50 mL). The chloroform was then dried over sodium sulfate and evaporated under reduced pressure. The acetate derivatives were subsequently analyzed by mass and proton magnetic resonance spectrometry and the spectra obtained supported the peracetylated structures.

Preparation of 3',4'-Dimethoxypropiophenone

This compound was prepared from 3',4'-dihydroxypropiophenone and propiovanillone by the alkylation method of Buck (61) using dimethyl sulfate. After recrystallization from ether-petroleum ether a white crystalline product was obtained: m.p. 59-60°C. Literature: m.p. 59-60°C (58). Yields of 85% were obtained.

Preparation of 4'-Benzyloxy-3'-methoxypropiophenone

A solution of 11.9356 g (0.06623 mole) of propiovanillone and 66.23 mL of 1N sodium hydroxide (0.06623 mole) was evaporated to dryness under reduced pressure. The solid was dissolved in 200 mL of N,N-dimethylformamide and 11.5 g (0.06656 mole) of benzyl bromide was added dropwise. The reaction was stirred for two hours and then 500 mL of distilled water was added. The emulsion was then extracted with chloroform (5 x 100 mL) and the combined chloroform extracts washed with 5% sodium hydroxide (3 x 100 mL) and distilled water (4 x 100 mL). The chloroform was dried over sodium sulfate and evaporated under reduced pressure to give a sirup. The sirup was crystallized from isopropanol to give 16.9 g (94.5% yield) of white crystalline material: m.p. 94.5-96°C. Literature: m.p. 92-94°C (62). ^{1}H PMR (60 MHz, $CDCl_3$): δ 1.20 (t, CH_3, 3H, J=7 Hz), 2.90 (q, CH_2, 2H, J=7 Hz), 3.92 (s, OCH_3, 3H), 5.20 (s, OCH_2, 2H), 6.90-7.45 (m, arom., 8H).

Preparation of 2-(2-Methoxy-4-methylphenoxy)propanoic Acid

This compound was prepared from ethyl-2-bromopropionate and creosol using the procedure of Avalaht and Fredga (63). After recrystallization from methanol a white crystalline material was obtained in 69% yield: m.p. 111.5-112°C. (Found: C, 62.85; H, 6.66. $C_{11}H_{14}O_4$ requires C, 62.84; H, 6.71%.) ^{1}H PMR (60 MHz, $CDCl_3$): δ 1.63 (d, CH_3, 3H, J=7 Hz), 2.30 (s, ϕ-CH_3, 3H), 3.85 (s, OCH_3, 3H), 4.63 (q, CH, 1H, J=7 Hz), 6.60-7.00 (m, arom., 3H), 10.23 (s, CO_2H, 1H).

Preparation of 2-(2-Methoxy-4-methylphenoxy)propanol

A solution of 5.0 g (0.0227 mole) of 2-(2-methoxy-4-methylphenoxy)propanoic acid in 100 mL of anhydrous ether was added dropwise to a stirred solution of 2.0 g of lithium aluminum hydride in 200 mL of anhydrous ether. After addition was completed, the solution was stirred an additional 4 hours. Ethyl acetate (50 mL) was added dropwise to consume excess reducing agent. After addition of 200 mL of distilled water, the layers were separated and the aqueous layer further extracted

with ether (3 x 50 mL). The combined ether layers were dried over sodium sulfate and evaporated under reduced pressure to give a colorless oil. The oil was distilled under vacuum: b.p. 85-86°C @ 0.025 mm Hg. ^{1}H PMR (60 MHz, $CDCl_3$): δ 1.30 (d, CH_3, 3H, J=6 Hz), 2.28 (s, ϕ-CH_3, 3H), 3.17 (s, OH, 1H), 3.63 (q, CH_2, 2H, J=5 Hz), 3.82 (s, OCH_3, 3H), 4.20 (m, CH, 1H), 6.60-7.00 (m, arom., 3H); 85% yield.

Preparation of 2-(2-Methoxy-4-methylphenoxy)propionaldehyde

To a stirred solution of 35 g of dipyridine chromium trioxide complex, prepared according to Collins and Hess (64), in 700 mL of anhydrous dichloromethane at 10°C was added 4 g of 2-(2-methoxy-4-methylphenoxy)propanol dissolved in 50 mL of anhydrous dichloromethane. The temperature was allowed to rise to room temperature and stirring continued for 1/2 hour. The solution was decanted and the black tar rinsed with dichloromethane (4 x 50 mL). The combined organic fractions were washed with 5% sodium hydroxide (3 x 100 mL), 5% hydrochloric acid (3 x 100 mL) and saturated sodium bicarbonate (3 x 100 mL). The organic fraction was then dried over sodium sulfate and evaporated under reduced pressure to give an orange oil. This oil was distilled under vacuum to give a colorless oil: b.p. 60-62°C @ 0.025 mm Hg. (Found: C, 68.03; H, 7.49. $C_{11}H_{14}O_3$ requires C, 68.02; H, 7.26%.) ^{1}H PMR (60 MHz, $CDCl_3$): δ 1.45 (d, CH_3, 3H, J=7 Hz), 2.30 (s, ϕ-CH_3, 3H), 3.83 (s, OCH_3, 3H), 4.48 (d, CH, 1H, J=1.5, 7 Hz), 6.60-7.00 (m, arom., 3H), 9.83 (d, CHO, 1H, J=1.5 Hz); 45% yield.

Preparation of 3',4'-Dimethoxy-2-(2-methoxy-4-methylphenoxy)propiophenone

To a solution of 3.215 g (0.0233 mole) of 2-methoxy-4-methyl phenol in 15 mL of methanol was added 23.1 mL of 1N (0.0231 mole) of sodium hydroxide. This was evaporated *in vacuo* at 30°C to a purple solid. Two 20-mL portions of 1,2-dichloroethane were also evaporated to remove any residual moisture. The sodium salt was dissolved in 100 mL of N,N-dimethylformamide and 6.3 g (0.0230 mole) of 2-bromo-3',4'-dimethoxypropiophenone added. The reaction was sealed with a drying tube

and heated on a steam bath for 2 hours. The solution was cooled, 200 mL of distilled water added and then extracted with chloroform (3 x 150 mL). The chloroform extracts were washed with 5% sodium hydroxide (3 x 150 mL) and distilled water (3 x 100 mL). The chloroform was then dried over sodium sulfate and evaporated to give a colorless sirup. The product was crystallized from ether-petroleum ether to give 6.8 g of white crystalline product. Yield 85%; m.p. 92-3°C. (Found: C, 67.34; H, 6.83. $C_{19}H_{20}O_5$ requires C, 69.07; H, 6.71%.) ^{1}H PMR (60 MHz, $CDCl_3$): δ 1.68 (d, γ-CH_3, 3H, J=7 Hz), 2.26 (s, ϕ-CH_3, 3H), 3.83, 3.95 (s, OCH_3, 9H), 5.40 (q, β-CH, 1H, J=7 Hz), 6.6-7.0 (m, arom., 4H), 7.7-8.0 (m, arom., 2H).

Preparation of 1-(3,4-Dimethoxyphenyl)-2-(2-methoxy-4-methylphenoxy)propanol

To a solution of 2.0 g (0.00578 mole) of 3',4'-dimethoxy-2-(2-methoxy-4-methylphenoxy)propiophenone in 150 mL of anhydrous ethanol was added 4.0 g of sodium borohydride and the solution stirred for 2 hours. To this was then added 200 mL of distilled water and the solution extracted with chloroform (3 x 100 mL). The chloroform was washed with distilled water (3 x 100 mL), dried over sodium sulfate and evaporated to a sirup. The compound was crystallized from ether-petroleum ether to give a crystalline hydrate, m.p. 67-71°C and subsequently to give a nonhydrated crystalline product of m.p. 85-86°C. (Found: C, 68.46; H, 7.29. $C_{19}H_{24}O_5$ requires C, 68.65; H, 7.23%.) ^{1}H PMR (60 MHz, $CDCl_3$): δ 1.17 (d, γ-CH_3, 3H, J=6.5 Hz), 2.33 (s, ϕ-CH_3, 3H), 3.50 (s, OH, 1H), 3.83 (s, OCH_3, 9H), 4.33 (m, β-CH, 1H), 4.85 (d, α-CH, 1H, J=4 Hz), 6.7-7.1 (m, arom., 6H).

PREPARATION OF PEROXYACETIC ACID

Passivation of Glassware

Peroxyacetic acid readily decomposes in the presence of contaminants such as heavy metal ions to acetic acid and hydrogen peroxide. To limit this effect, glassware used with PA solutions was passivated by the following procedure out-

lined by the FMC Corporation (65).

1. Degreasing and washing with Alconox.
2. Distilled water rinse.
3. 15-Minute soak with 0.5% sodium hydroxide.
4. Distilled water rinse.
5. 45-Minute soak with 35% nitric acid.
6. Distilled water rinse.
7. Overnight soak in 30% hydrogen peroxide.
8. Distilled water rinse.

Peroxyacetic Acid Generation

To prevent excess decomposition of the peroxyacetic acid solutions, all glassware for storage and transferral of PA was passivated prior to use. The PA was generated by the sulfuric acid-catalyzed hydrogen peroxide oxidation of acetic acid following a procedure detailed by the FMC Corporation (65). The initial charge for the reactor was distilled water, 114 g, concentrated sulfuric acid, 115 g, glacial acetic acid, 51.2 g, 50% hydrogen peroxide, 270 g, and dipicolinic acid, 0.275 g. The feed solution was comprised of distilled water, 118 g, glacial acetic acid, 88 g, and 50% hydrogen peroxide, 95 g. The operating conditions for the generator were:

Bath temperature: 75-80°C

Reactor temperature: 45°C

Vapor temperature: 53-57°C

Pressure: 40-50 mm Hg

These conditions typically produced 300 g of 30-40% PA that was diluted to approximately 20% PA with glacial acetic acid and stored in a refrigerator until needed.

Standardization of Sodium Thiosulfate

Sodium thiosulfate solutions used for titration of PA were standardized against Primary Standard Grade potassium dichromate (Baker) using the following procedure (66).

An accurately weighed sample, w, (0.21-0.22 g) of potassium dichromate was transferred quantitatively to a 500-mL Erlenmeyer flask. The sides of the flask were wetted; the solution diluted to 125 mL and 5 g of potassium iodide added. After dissolution of the iodide was complete, 5 mL of 6N hydrochloric acid was added with constant swirling. The sides of the flask were carefully rinsed down so that a layer of distilled water remained above the solution. The flask was stoppered and stored in the dark for about 6 minutes. A final 165 mL of distilled water was added and the solution titrated with thiosulfate solution, adding starch near the end point. The following calculation gives the normality of the thiosulfate:

$$N = \frac{\text{wt. of } K_2Cr_2O_7 \text{ [w(in mg)]}}{(\text{mL of titrant})(49.04)}$$

Analysis of Peroxyacetic Acid

The method of Sully and Williams (67) was used in this thesis. One-hundred milliliters of 0.1N acetic acid was placed in a 500-mL Erlenmeyer flask and cooled to 5° in an ice-water bath. An accurately weighed sample of PA solution (w) was then added to the flask. Ten milliliters of 15% KI was added and a stopwatch started. The initial buret reading (x_i) was recorded and the liberated iodine was titrated with 0.1N sodium thiosulfate. Near the end point, 5-10 drops of starch indicator was added. The solution was minimally overtitrated and the buret reading x_1 and time of return of blue color t_1 were noted. The overtitration was repeated once more and the second buret reading x_2 and time for the blue color to return (t_2) were noted. Ten drops of saturated ammonium molybdate

solution was added and the titration continued to a final end point (x_f). The concentrations of peroxyacetic acid and hydrogen peroxide were calculated based on the following equations:

$$\text{Peroxyacetic acid at time zero} = x_0 = x_1 - \frac{t_1(x_2-x_1)}{t_2-t_1}$$

$$\% \text{ PA} = 3.803\ (x_0-x_1)(\text{N of } N_2S_2O_3)/w$$

$$\% H_2O_2 = 1.701\ (x_f-x_0)(\text{N of } Na_2S_2O_3)/w$$

PEROXYACETIC ACID OXIDATION OF MODEL COMPOUNDS

REACTION CONDITIONS

Prior to each oxidation, peroxyacetic acid was freshly generated. The generator solution was diluted to approximately 20% peroxyacetic acid with glacial acetic acid and stored at 5°C. The use of freshly prepared peroxyacetic acid kept the amount of hydrogen peroxide at very low levels.

The oxidations were run in glass stoppered passivated round bottom flasks. The substrate was added to the flask and an appropriate amount of glacial acetic acid was added. This solution was stored in a constant temperature bath for one-half hour to effect solution of the substrate. At this time an appropriate amount of the 20% PA solution was added, the solution swirled and a time zero sample was taken for initial peroxyacetic acid and substrate concentrations. A control was run using the same amounts of peroxyacetic acid solution and glacial acetic acid to determine the degradation of the PA solution during the time of the oxidation.

SAMPLE WORKUP PROCEDURES

At the desired time, aliquots of the oxidation solution were removed from the reaction flask and placed in preweighed vials. For PA determinations, duplicate 1-mL aliquots were withdrawn, weighed and titrated as previously described. A flow chart showing the workup procedure for the PA oxidation of β-ether XXXVI is shown in Fig. 53.

For analysis of starting material in PA oxidations of β-ether XXXVI, duplicate 1-mL aliquots were withdrawn, weighed and a minimum of sodium sulfite added to reduce excess PA. Starch-potassium iodide test strips were used to detect residual PA. An appropriate amount of the internal standard solution was pipeted into the vial and the contents of the vial transferred to a 60-mL separatory funnel. Chloroform (20 mL) was added and the solution extracted with 5% sodium carbonate (3 x 20 mL) and distilled water (3 x 20 mL). The chloroform layer was then dried over sodium sulfate and evaporated under reduced pressure. The resulting sirup was transferred with chloroform to a vial, concentrated under reduced pressure and then analyzed by GLC.

For the analysis of starting material for the PA oxidation of diol XL or ketol XLI, the samples were withdrawn at appropriate times and the residual PA reduced with a minimum of sodium sulfite. Internal standard was added and the samples were neutralized to pH 7-7.5 with saturated sodium carbonate while bubbling nitrogen through the samples. The solutions were then extracted with chloroform (8 x 25 mL) and the chloroform extracts combined, dried over sodium sulfate and evaporated under reduced pressure. Residual water was removed by evaporating with two successive 10-mL portions of 1,2-dichloroethane. The samples were then transferred to a septum cap vial with 0.3 mL of anhydrous chloroform. Trisil concentrate, 0.4 mL, was added, the solution allowed to react for 30 minutes and then analyzed by gas chromatography.

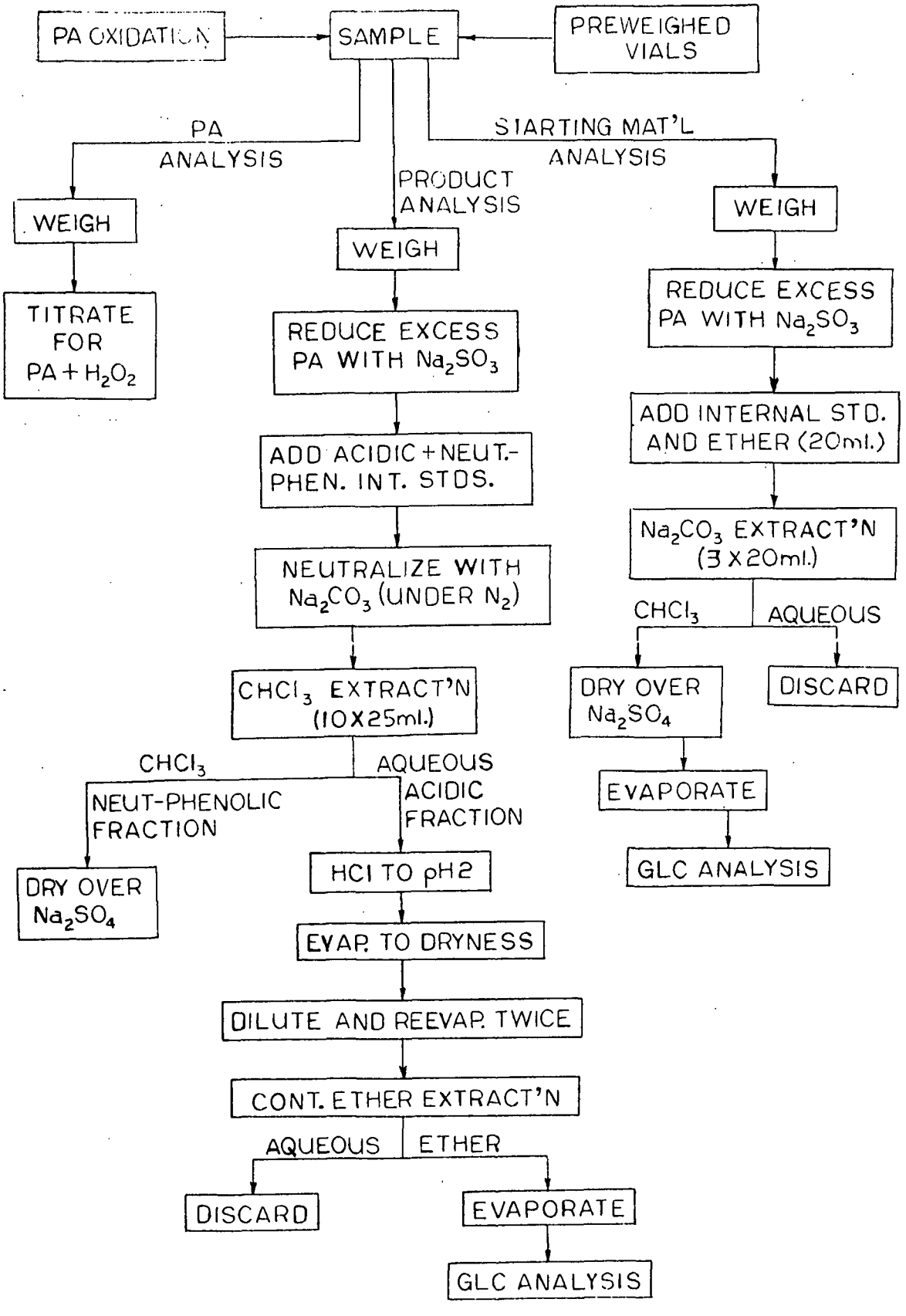


Figure 53. Flow Chart of Workup Procedures Used for Peroxyacetic Acid Oxidations of Model Compounds

For product analysis of β-ether XXXVI, duplicate 5-mL aliquots were withdrawn, weighed and excess PA reduced with a minimum of sodium sulfite as indicated by starch-potassium iodide test paper. Appropriate amounts of neutral-phenolic and acidic internal standards were pipeted into the vial and the samples transferred to a beaker. Nitrogen gas was bubbled through the solutions and the samples neutralized with saturated sodium carbonate to a pH 7.2-7.5.

The samples were then extracted with chloroform (10 x 25 mL). The chloroform extracts, containing the neutral and phenolic products, were combined, dried over sodium sulfate and evaporated under reduced pressure to yellow-orange oils. The aqueous phase was acidified with concentrated hydrochloric acid to pH 2 and evaporated to dryness under reduced pressure at 30°C. The samples were subsequently diluted two times with water and evaporated to dryness. The samples were then diluted with 100-125 mL of distilled water and continuously extracted with ether for 24-36 hours. The ether layer which contained the acidic products was then evaporated under reduced pressure to dryness.

The neutral and phenolic products were dissolved in 0.2-0.4 mL of anhydrous chloroform and transferred to septum top vials. Tri-sil concentrate, 0.3-0.7 mL, was added and the solution allowed to react for 1 hour. The acidic products were dissolved in 0.2-0.4 mL of silylation grade, N,N-dimethyl formamide (Pierce Chem. Co.) and 75-150 µliters of N,O-bis-trimethylsilyltrifluoroacetamide (BSTFA) was added. The solution was allowed to react for 1 hour prior to injection.

For qualitative identification of PA oxidation products of β-ether XXXVI, 2.9435 g (0.0886 mole) of XXXVI were oxidized for 24 hours as previously described. The entire sample was worked up as shown in Fig. 53 for product analysis. Subsequently, the neutral-phenolic and acidic fractions were chromatographed on a silica gel column (50 x 1000 mm). For the neutral and phenolic products, the eluants used were benzene, isopropyl ether, ethyl ether, chloroform, ethyl

acetate, and acetone. For the acidic fraction the eluants used were ethyl ether: chloroform (1:1, v/v), chloroform, ethyl acetate, acetone, ethanol, distilled water:acetic acid (1:1, v/v). The first two fractions of neutral-phenolic column effluent were subsequently analyzed as is, and all other fractions were derivatized with trimethylsilyl reagents as previously described. The fractions were fractionated by preparative GLC and the separate fractions subsequently analyzed by PMR and mass spectrometry. The retention times of the various components were measured using the same conditions as previously described for product analysis.

The fraction containing oxidation product XXXVII was analyzed by TLC using isopropyl ether:ethyl ether (1:1, v/v). Oxidation product XXXVII gave the same R_f value (0.67) as a known sample of 3',4'-dimethoxy-2-(2-methoxy-4-methylphenoxy)propiophenone. In addition, the same color reaction to the spray reagents previously described were shown by oxidation product XXXVI and the known sample.

The sample containing oxidation product XL was evaporated to dryness. An aliquot was used for preparative GLC and subsequent PMR and MS spectral analyses. The remainder of the sample was taken up in a minimum of ethyl acetate and gave a white crystalline product. This product was recrystallized from ethyl acetate and gave m.p. 122-123°C, identical to that for erythro 1-(3,4-dimethoxyphenyl)-propan-1,2-diol (38). The sample was also analyzed by infrared spectrophotometry as a KBr pellet.

ACKNOWLEDGMENTS

The author expresses his gratitude to Drs. R. D. McKelvey, D. Johnson, and E. Malcolm for their interest and guidance while serving as members of his Thesis Advisory Committee. In particular, the author sincerely appreciates the assistance and encouragement of Drs. R. D. McKelvey and D. Johnson during the study and for their advice in the preparation of this manuscript. The author is also grateful to E. E. Dickey for his assistance during the initial stages of this work and continued interest in the course of this study.

To the other faculty members, staff personnel and fellow students who contributed in many ways, the author expresses his thanks.

The generous support provided by The Institute of Paper Chemistry and the member companies which provide this support, is gratefully acknowledged.

For their continual interest and encouragement, the author expresses a special thanks to his parents and my wife's parents.

For her assistance in the preparation of this manuscript, her encouragement and sacrifices, I am deeply indebted to my wife, Judy.

LITERATURE CITED

1. Giguere, P. A. and Olmas, A. W., Can. J. Chem. 30:821(1952).

2. Davison, W. H. T., J. Chem. Soc. 1951:2456.

3. Swern, D. Organic Peroxides. Vol. 2. New York, Wiley-Interscience, 1970.

4. Poljak, A., Angew. Chem. 60:45(1948).

5. Thompson, N. S. and Kaustinen, O. A., Tappi 47:157(1964).

6. Leopold, B., Tappi 44:230(1961).

7. Ishikawa, H., Okubo, K., and Oki, T., Appl. Polymer Symp. 28:1169(1976).

8. Swern, D. Organic Reactions. Vol. 7. p. 378-433. New York, J. Wiley and Sons, Inc., 1953.

9. Hassall, L. H. Organic Reactions. Vol. 9. p. 73-106. New York, J. Wiley and Sons, Inc., 1957.

10. Swern, D., Chem. Rev. 45:1-68(1949).

11. Hawthorne, M. F., Emmons, W. D., and McKallum, K. S., J. Am. Chem. Soc. 80:6393(1958).

12. Doering, W. L. and Speers, L., J. Am. Chem. Soc. 72:5515(1950).

13. Friess, S. L. and Soloway, A. H., J. Am. Chem. Soc. 73:3968(1951).

14. Ross, D. R., Gebhart, N., and Gerecht, R., J. Am. Chem. Soc. 67:1275(1945).

15. Elvidge, J. A., Linstead, R. P., and Sims, P., J. Chem. Soc. 1951:3398-402.

16. Hine, J. Physical Organic Chemistry. 3rd ed. pp. 87, 372. New York, McGraw-Hill, 1956.

17. Boeseken, J., Proc. Acad. Sci., Amsterdam 35:70(1932).

18. Wocek, A. and Fiedler, R., Monatsch. 80:170(1949).

19. Farrand, J. C. The peroxyacetic acid oxidation of 4-methylphenols and their methyl ethers. Doctoral Dissertation. Appleton, Wis., The Institute of Paper Chemistry, 1969. 206 p.

20. Friess, S. L., Soloway, A. H., Morse, B. K., and Ingersoll, W. C., J. Am. Chem. Soc. 74:1305-9(1952).

21. Davidge, H., Davies, A. G., Kenyon, J., and Mason, R. F., J. Chem. Soc. 1958:4569-73.

22. Chambers, R. D., Googin, P., and Musgrave, W. K. R., J. Chem. Soc. 1959: 1804-7.

23. Bryce-Smith, D. and Gilbert, A., J. Chem. Soc. 1964:873.

24. Hatakeyama, H., Nakano, J., and Migita, N., J. Chem. Soc. Japan, Ind. Chem. Sect. 68:972(1965).

25. Ishikawa, H., Oki, T., and Okubo, K., Japan Tappi 20:435(1966).

26. Oki, T., Okubo, K., and Ishikawa, H., J. Jap. Wood Res. Soc. 20:89(1974).

27. Kinoshita, Y., Oki, T., and Ishikawa, H., J. Jap. Wood Res. Soc. 13:319 (1967).

28. Lundquist, K. and Hedlund, K., Acta Chem. Scand. 21:1750-4(1967).

29. Oki, T., Okubo, K., and Ishikawa, H., J. Jap. Wood Res. Soc. 18:601 (1972).

30. Oki, T., Okubo, K., and Ishikawa, H., J. Jap. Wood Res. Soc. 20:549-57 (1974).

31. Sakai, K., Kuroda, K., and Kishimoto, S., Tappi 55:1702-6(1972).

32. Sarkanen, K. V. and Lai, Y. Z. Isolation and Structural Studies. In Sarkanen and Ludwig's Lignins. New York, John Wiley and Sons, Inc., 1971.

33. Sakai, K. and Kondo, T., J. Jap. Wood Res. Soc. 21:39-42(1975).

34. Sakai, K. and Kondo, T., J. Jap. Wood Res. Soc. 21:87-92(1975).

35. Fleck, J. A. The investigation of peracetic acid-oxidized loblolly pine by pyrolysis-gas chromatography-mass spectrometry. Doctoral Dissertation. Appleton, Wis., The Institute of Paper Chemistry, 1975. 214 p.

36. Sarkanen, K. V. and Wallis, A. F. A., J. Chem. Soc. Perkins Trans. I, 1973: 1869-78.

37. Adler, E., Delin, S., and Miksche, G. E., Acta Chem. Scand. 20:1035-7(1966).

38. March, J. Advanced Organic Chemistry: Reactions, Mechanisms and Structures. p. 265. New York, N.Y., McGraw-Hill, 1968.

39. Kratzl, K., Kisser, W., Gratzl, J., and Silbernagel, H., Monatsch. Chem. 90: 771(1959).

40. Sarkanen, K. V. and Dence, C. W., Tappi 43:87(1960).

41. Boeseken, J. and Jacobs, F., Rec. Trav. Chem. 55:804(A36)(----).

42. Mieland, M. and Mischer, K. F., Helv. Chim. Acta 32:1768(1949).

43. Rapson, H. and Strumila, G., Pulp Paper Mag. Can. 76:T276-80(1975).

44. Hatakeyama, H., Nakano, J., and Migita, N., J. Chem. Soc. Japan, Ind. Chem. Sect. 70:957(1967).

45. Yamaguchi, A., Hiroi, T., and Miyazaki, M., J. Jap. Wood Res. Soc. 15:256-61 (1969).

46. Silverstein, R. M. and Bassler, G. C. Spectrometric Identification of Organic Compounds. New York, J. Wiley and Sons, Inc., 1967. 256 p.

47. Budzikiewicz, H., Djerassi, C., and Williams, D. H. Mass Spectrometry of Organic Compounds. San Francisco, Calif., Holden-Day, Inc., 1967. 690 p.

48. Yamamoto, O., Hiyamizu, K., Sekine, K., and Funihara, S., Anal. Chem. 44: 1794(1972).

49. Blatchly, J. M., Green, R. J., and McOmie, J. F., J. Chem. Soc. Perkin Trans. I, 1972:2286.

50. Swinehart, J. S. Organic Chemistry: An Experimental Approach. p. 418. New York, Meredith, 1969.

51. Lund, H. and Bjerrum, J., Ber. 64:210(1931).

52. Perrin, D. D., Armarego, W. L. F., and Perrin, D. R. Purification of Laboratory Chemicals. New York, Pergamon Press, 1966. 362 p.

53. Reynolds, D. D. and Evans, W. F., J. Am. Chem. Soc. 60:2559-61(1938).

54. Bailey, C. W. and Dence, C. W., Tappi 52:498(1969).

55. Adler, E. and Magnusson, R., Acta Chem. Scand. 13:519(1959).

56. Boescher, J. and Greup, J., Rec. Trav. Chim. 58:528-37(1939).

57. Hibbert, H., Eastham, A., Fisher, H., and Kulka, M., J. Am. Chem. Soc. 66:605(1944).

58. Hibbert, H., Cramer, A. B., and Hunter, H., J. Am. Chem. Soc. 61:509-16(1939).

59. Baker, S. B., Evans, T. H., and Hibbert, H., J. Am. Chem. Soc. 70:60-3(1948).

60. Ludwig, C. H., Nist, B. J., and McCarthy, J. L., J. Am. Chem. Soc. 86:1186-96(1964).

61. Buck, J. S. Organic Syntheses. Coll. Vol. 2. p. 619-21. New York, J. Wiley and Sons, Inc., 1943.

62. Sundholm, F., Soc. Sci. Fennica, Comm. Phys. Math. 30:10(1965).

63. Avalaht, I. and Fredga, A., Arkiv. Kemi. 24:428(1965).

64. Collins, J. W. and Hess, R., Organic Syntheses 52:5(1972).

65. FMC Corporation. The operation of a bench scale peracetic acid generator. New York, FMC Corporation, 1963.

66. Kolthoff, I. M. and Belcher, R. Volumetric Analysis. Vol. III. p. 239. New York, Interscience Publishers, 1957.

67. Sully, B. D. and Williams, P. L., The Analyst 87:653-7(1962).

APPENDIX I

PROTON MAGNETIC RESONANCE SPECTRA OF OXIDATION PRODUCTS

Index to PMR Spectra

*Comparison made with PMR spectra of known compound.

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
a)	-0.10	Sing.	-	9
b)	0.05	Sing.	-	9
c)	1.21	Doub.	6	3
d)	3.85	Mult.	-	d+e = 7
e)	3.89	Sing.	-	
f)	4.31	Doub.	6	1
g)	6.8-6.95	Mult.	-	3

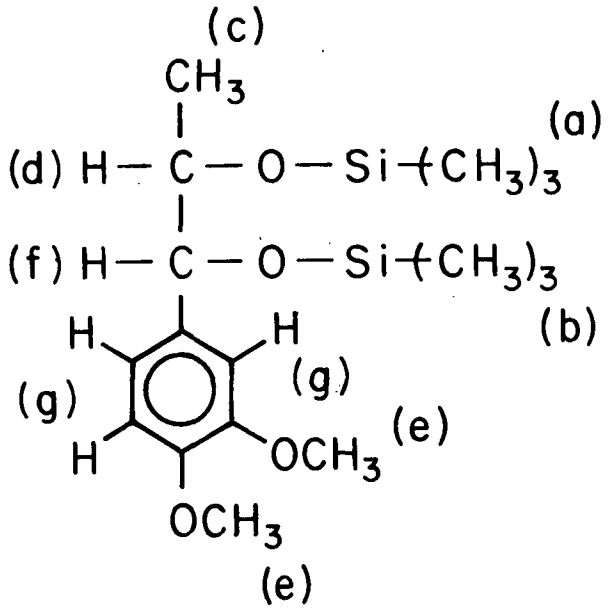


Figure 54. Structure and PMR Spectrum of bis-TMS Ether of Oxidation Product XLa

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
a)	0.12	Sing.	-	9
b)	2.08	Sing.	-	3
c)	3.87	Sing.	-	6
d)	4.99	Sing.	-	1
e)	6.7-6.9	Mult.	-	3

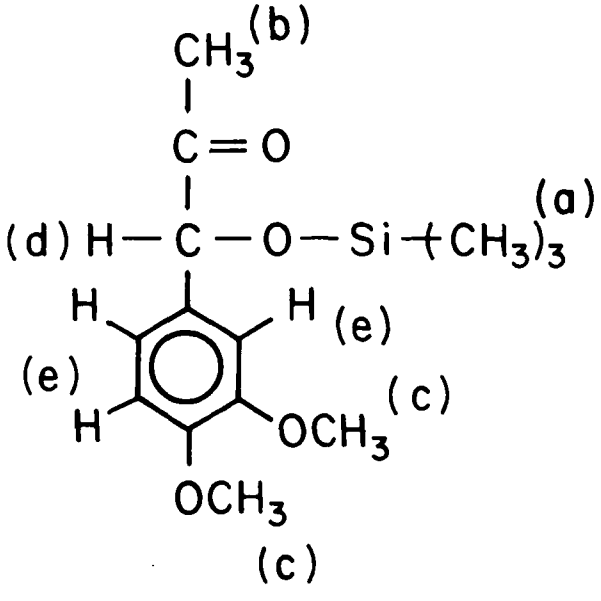


Figure 55. Structure and PMR Spectrum of TMS Ether of Oxidation Product XLI

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
a)	0.25	Sing.	-	9
b)	3.82	Sing.	-	3
c)	3.84	Sing.	-	3
d)	6.2-6.8	Mult.	-	3

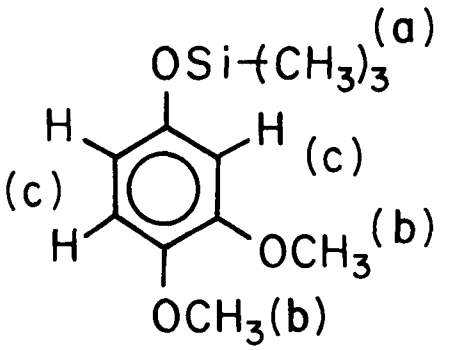


Figure 56. Structure and PMR Spectrum of TMS Ether of Oxidation Product XLII

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
Authentic sample of 3,4-dimethoxybenzaldehyde				
a)	3.94	Sing.	-	3
a)	3.97	Sing.	-	3
b)	6.8-7.6	Mult.	-	3
c)	9.82	Sing.	-	1
Oxidation Product XLIV				
a)	3.95	Sing.	-	3
a)	3.97	Sing.	-	3
b)	6.8-7.6	Mult.	-	3
c)	9.84	Sing.	-	1

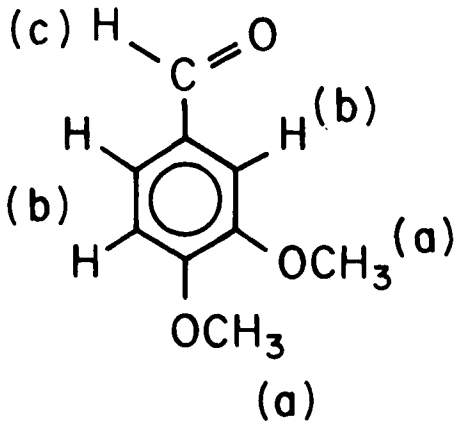


Figure 57. Structure and PMR Spectra of 3,4-Dimethoxybenzaldehyde and Oxidation Product XLIV

Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
Authentic sample of 2-(2-methoxy-4-methylphenoxy)propionaldehyde			
a) 1.43	Doub.	6	3
b) 2.33	Sing.	-	3
c) 3.83	Sing.	-	3
d) 4.47	Oct.	6,2	1
e) 6.7-6.9	Mult.	-	3
f) 9.83	Doub.	2	1
Oxidation Product XLV			
a) 1.46	Doub.	6	3
b) 2.31	Sing.	-	3
c) 3.84	Sing.	-	3
d) 4.47	Oct.	6,2	1
e) 6.7-6.9	Mult.	-	3
f) 9.80	Doub.	2	1

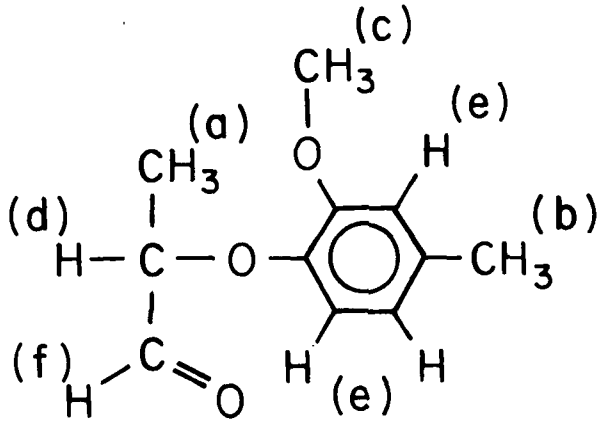


Figure 58. Structure and PMR Spectra of 2-(2-Methoxy-4-methylphenoxy)propionaldehyde and Oxidation Product XLV

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
		Authentic sample of di-O-acetylmethoxy-p-hydroquinone		
a)	2.29	Sing.	-	3
a)	2.30	Sing.	-	3
b)	3.81	Sing.	-	3
c)	6.6-7.1	Mult.	-	3
		Oxidation Product L		
a)	2.29	Sing.	-	3
a)	2.30	Sing.	-	3
b)	3.80	Sing.	-	3
c)	6.6-7.1	Mult.	-	3

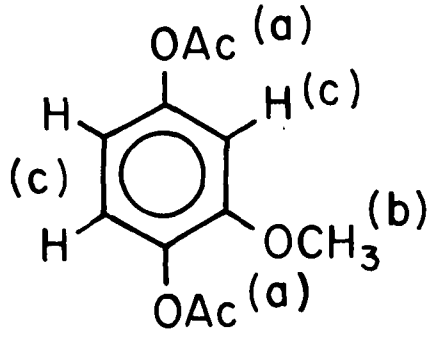


Figure 59. Structure and PMR Spectra of di-O-Acetylmethoxy-p-hydroquinone and Oxidation Product L

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
		Authentic sample of 3,4-dimethoxyphenyl acetate		
a)	2.28	Sing.	-	3
b)	3.84	Sing.	-	3
b)	3.86	Sing.	-	3
c)	6.1-6.9	Mult.	-	3
		Oxidation Product LIII		
a)	2.28	Sing.	-	3
b)	3.85	Sing.	-	3
b)	3.86	Sing.	-	3
c)	6.1-6.9	Mult.	-	3

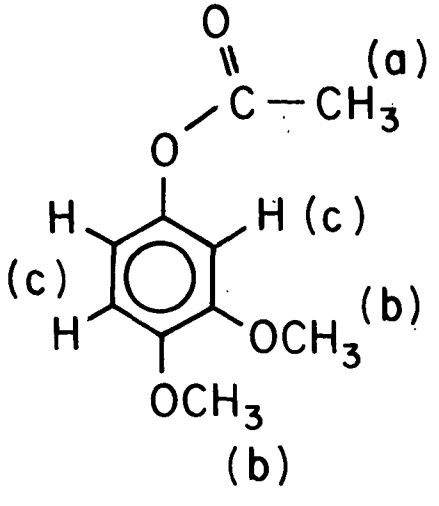


Figure 60. Structure and PMR Spectra of 3,4-Dimethoxyphenyl Acetate and Oxidation Product LIII

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
		Authentic sample of 2-methoxy-4-methylphenol (creosol)		
a)	2.25	Sing.	-	3
b)	3.80	Sing.	-	3
c)	5.53	Sing.	-	1
d)	6.5-6.9	Mult.	-	3
		Oxidation Product LIV		
a)	2.27	Sing.	-	3
b)	3.82	Sing.	-	3
c)	5.52	Sing.	-	1
d)	6.5-6.9	Mult.	-	3

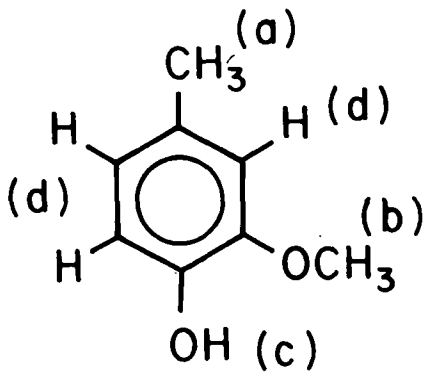


Figure 61. Structure and PMR Spectra of 2-Methoxy-4-methyl-phenol and Oxidation Product LIV

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
a)	0.28	Sing.	-	7
b)	2.29	Sing.	-	3
c)	3.86	Sing.	-	3
d)	6.6-6.9	Mult.	-	3

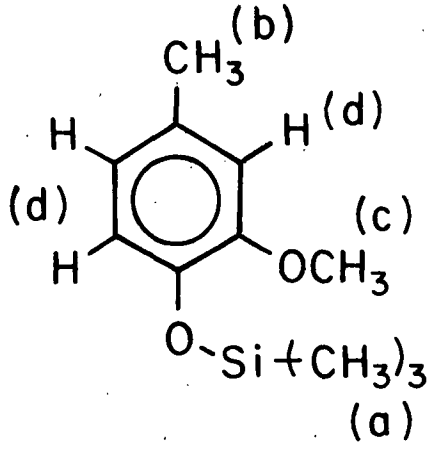


Figure 62. Structure and PMR Spectrum of TMS Ether of Oxidation Product LIV

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
		Authentic sample of 2-methoxy-4-methylphenyl acetate		
a)	2.29	Sing.	-	3
b)	2.34	Sing.	-	3
c)	3.80	Sing.	-	3
d)	6.65-6.95	Mult.	-	3
		Oxidation Product LV		
a)	2.29	Sing.	-	3
b)	2.34	Sing.	-	3
c)	3.79	Sing.	-	3
d)	6.65-6.95	Sing.	-	3

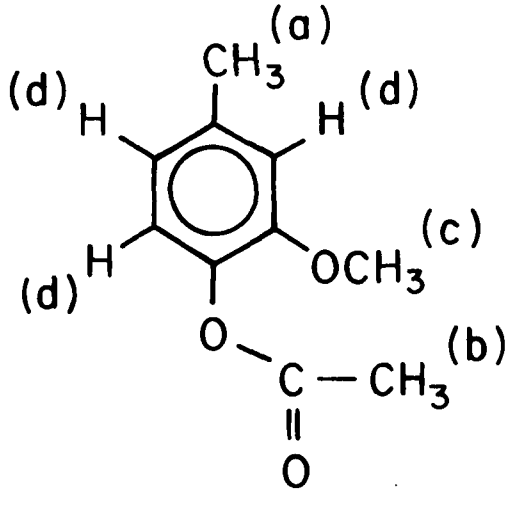


Figure 63. Structure and PMR Spectra of 2-Methoxy-4-methylphenyl Acetate and Oxidation Product LV

	Chemical Shift (ppm)	Peak Type	J (Hz)	No. of Protons
	Reported PMR spectrum for 5-carboxymethyl-4-methyl-2(5H)furanone (19)			
a)	1.57	Sing.	-	3
b)	2.69	Doub.	15	1
c)	2.91	Doub.	15	1
d)	3.68	Sing.	-	3
e)	6.03	Doub.	6	1
f)	7.65	Doub.	6	1
	Oxidation Product LX			
a)	1.57	Sing.	-	3
b)	2.64	Doub.	16	1
c)	2.95	Doub.	16	1
d)	3.70	Sing.	-	3
e)	6.05	Doub.	6	1
f)	7.68	Doub.	6	1

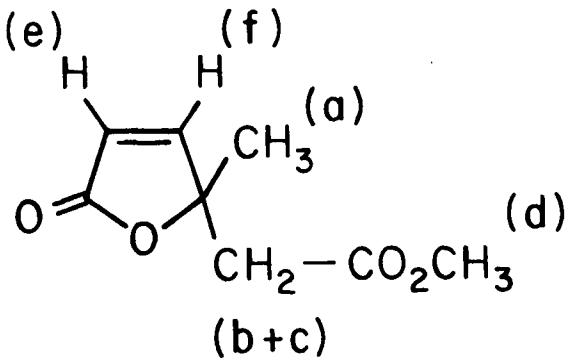


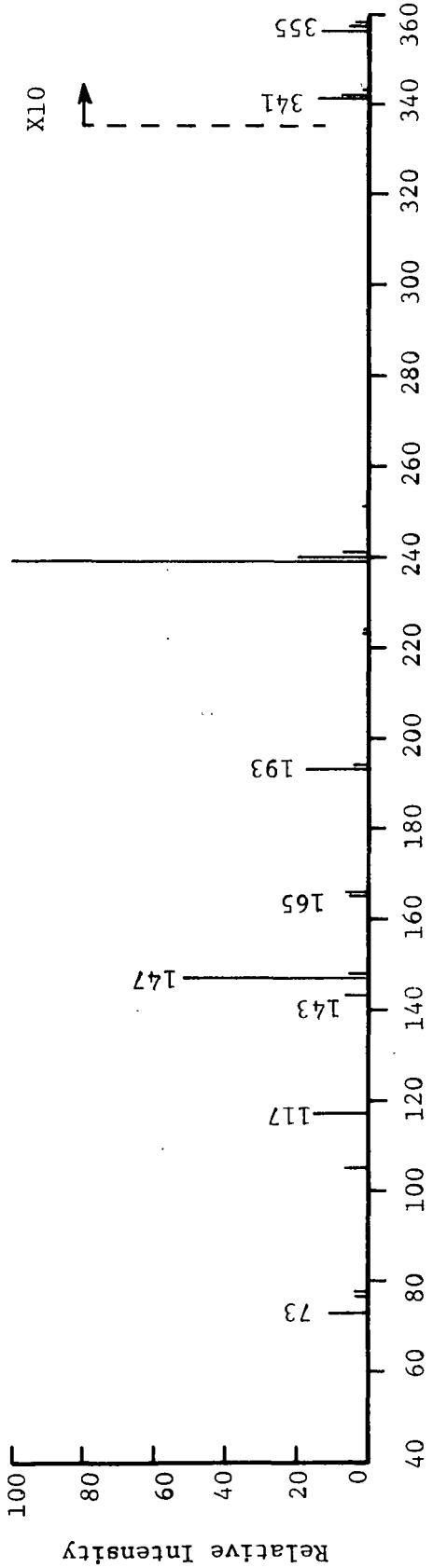
Figure 64. Structure and PMR Spectra of 5-Carboxymethyl-4-methyl-2(5H)furanone (19) and Oxidation Product LX

APPENDIX II

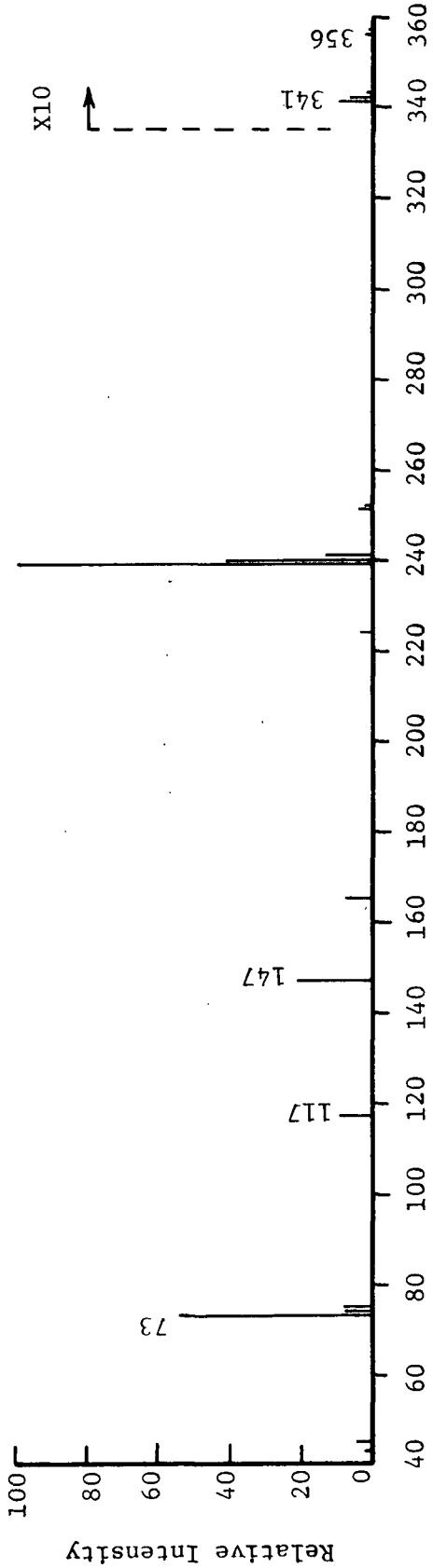
MASS SPECTRA OF OXIDATION PRODUCTS*

Index to Mass Spectra

*Mass spectra are compared with mass spectra of known compounds.

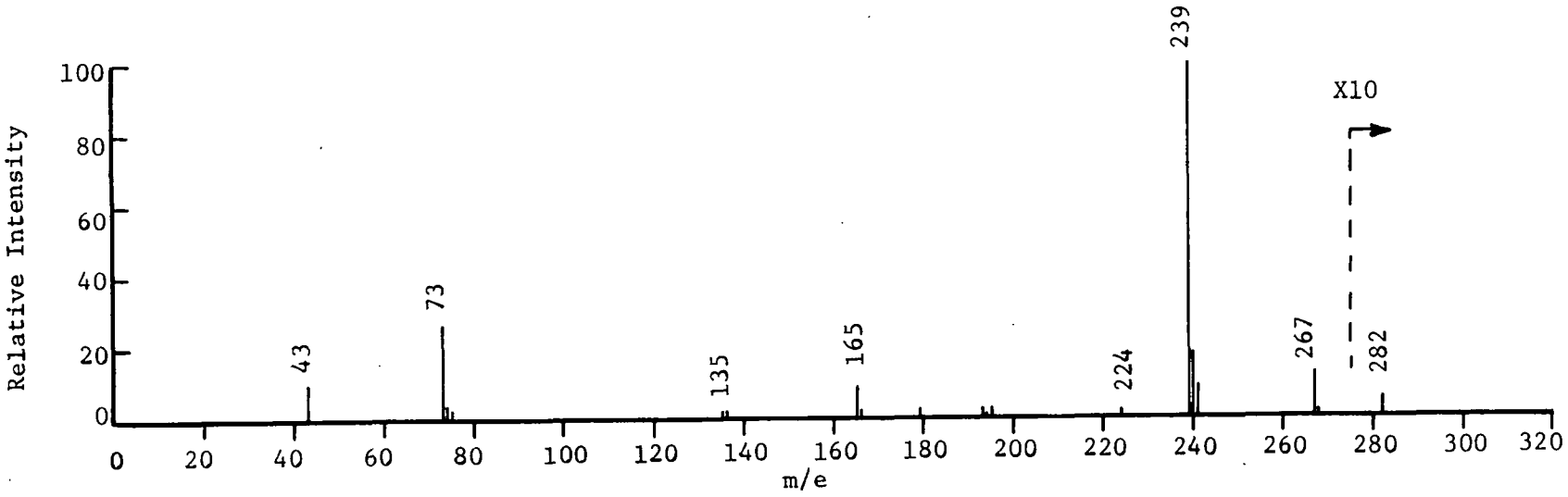


Mass spectrum of bis-TMS ether of oxidation product XLa

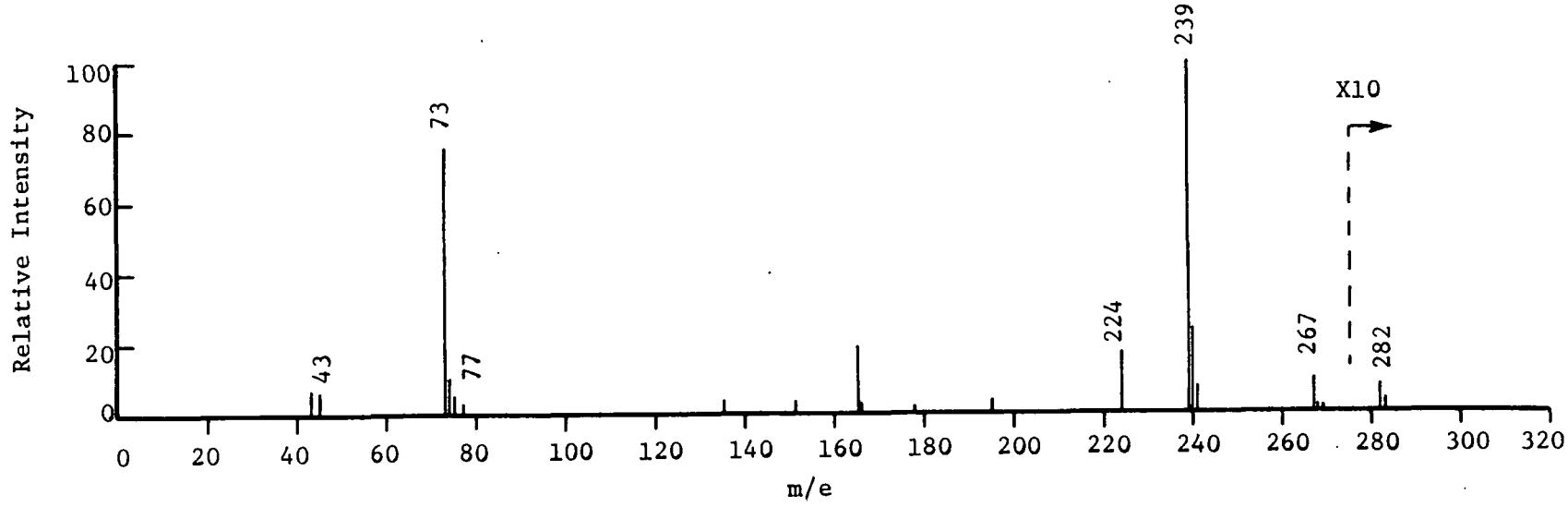


Mass spectrum of TMS derivative of 1-(3,4-dimethoxyphenyl)-propan-1,2-diol

Figure 65. Mass Spectra of bis-TMS Ethers of 1-(3,4-Dimethoxyphenyl)propan-1,2-diol and Oxidation Product XLa

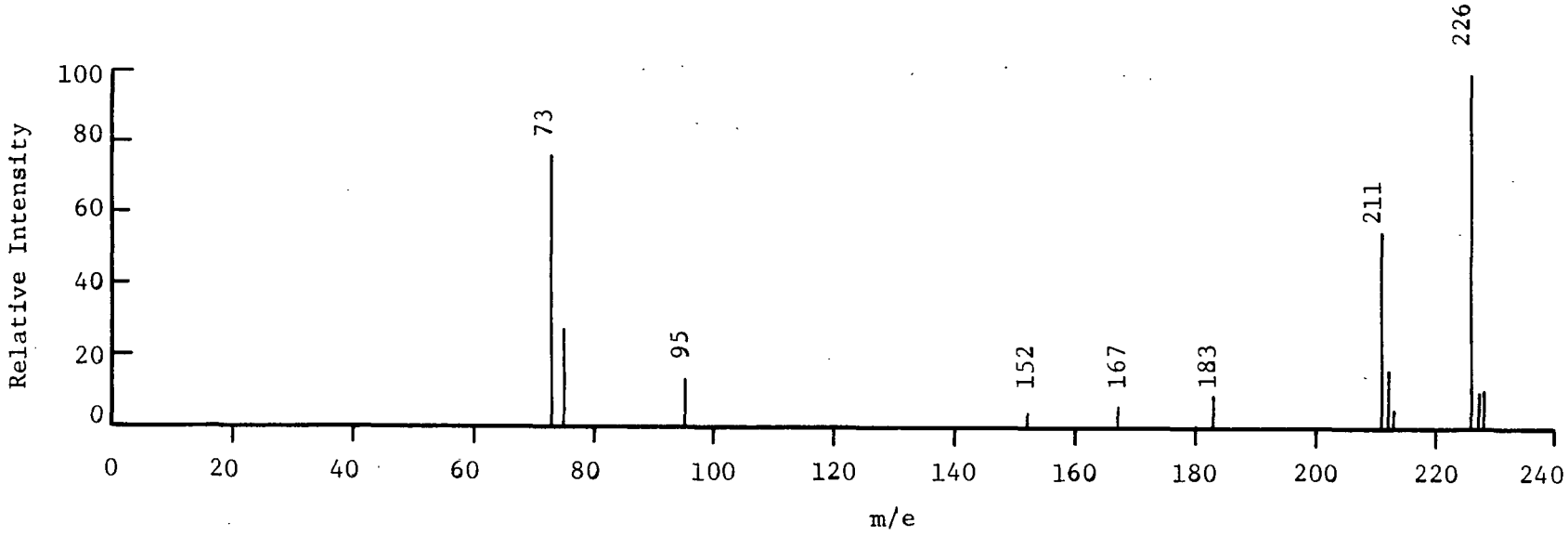


Mass spectrum of TMS ether of oxidation product XLI

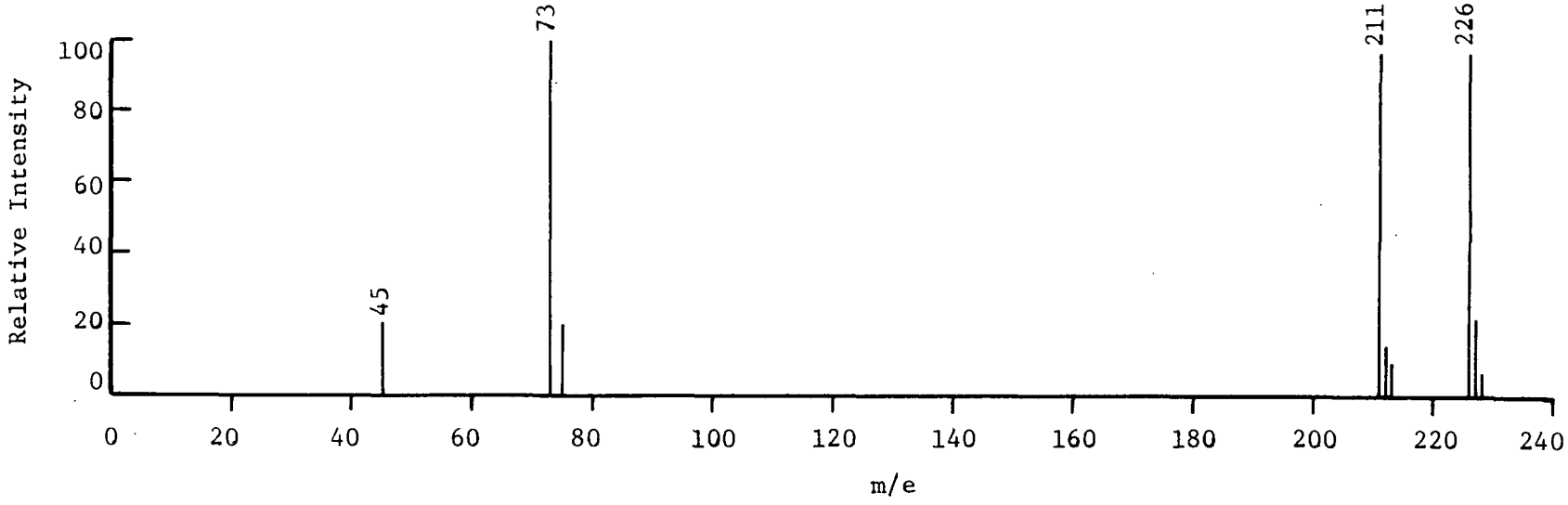


Mass spectrum of 1-[3,4-dimethoxyphenyl]-1-hydroxypropan-2-one

Figure 66. Mass Spectra of TMS Ethers of 1-(3,4-Dimethoxyphenyl)-1-hydroxypropan-2-one and Oxidation Product XLI



Mass spectrum of TMS ether of oxidation product XLII



Mass spectrum of TMS ether of 3,4-dimethoxyphenol

Figure 67. Mass Spectra of TMS Ethers of 3,4-Dimethoxyphenol and Oxidation Product XLII

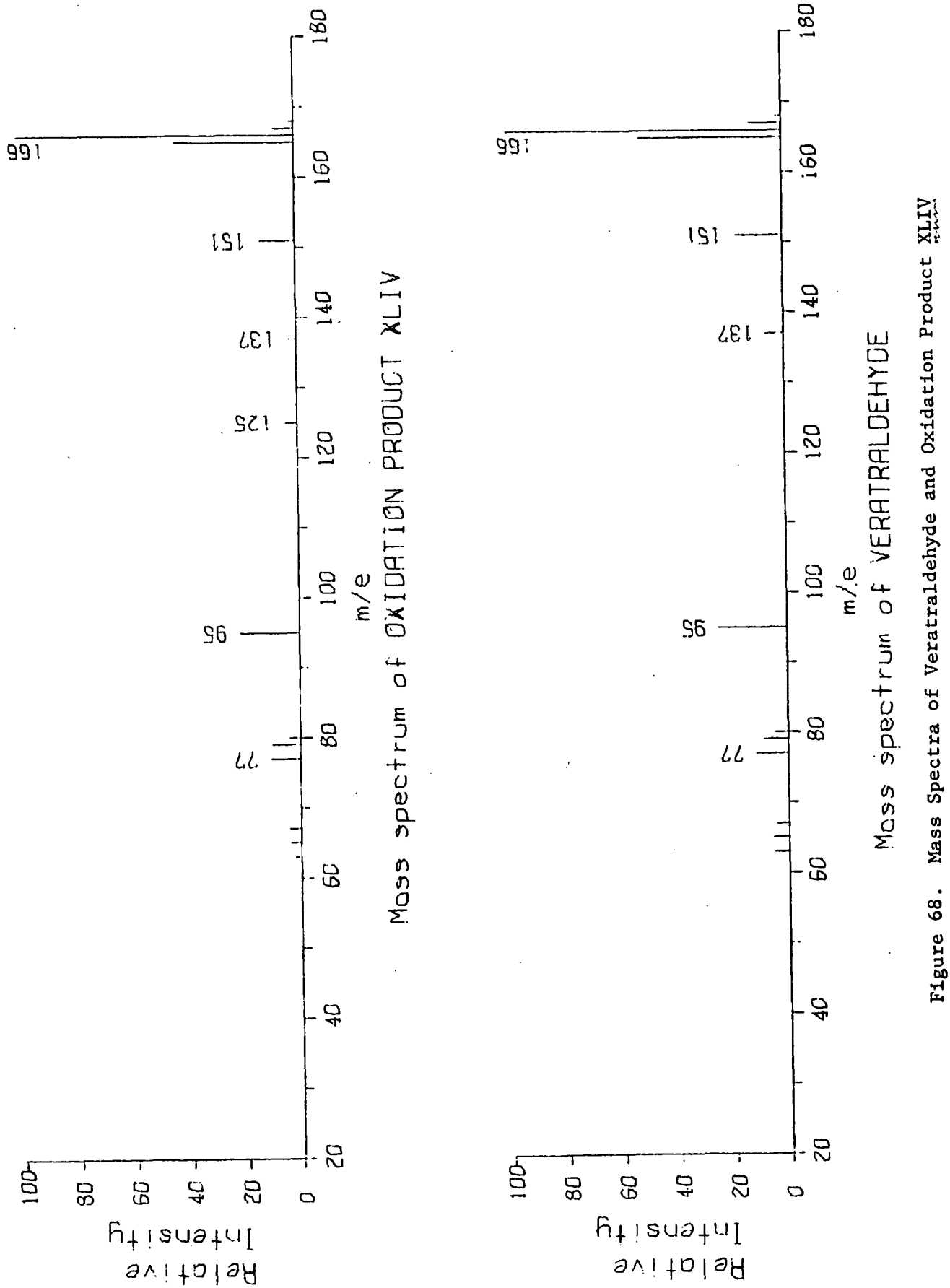


Figure 68. Mass Spectra of Veratraldehyde and Oxidation Product XLIV

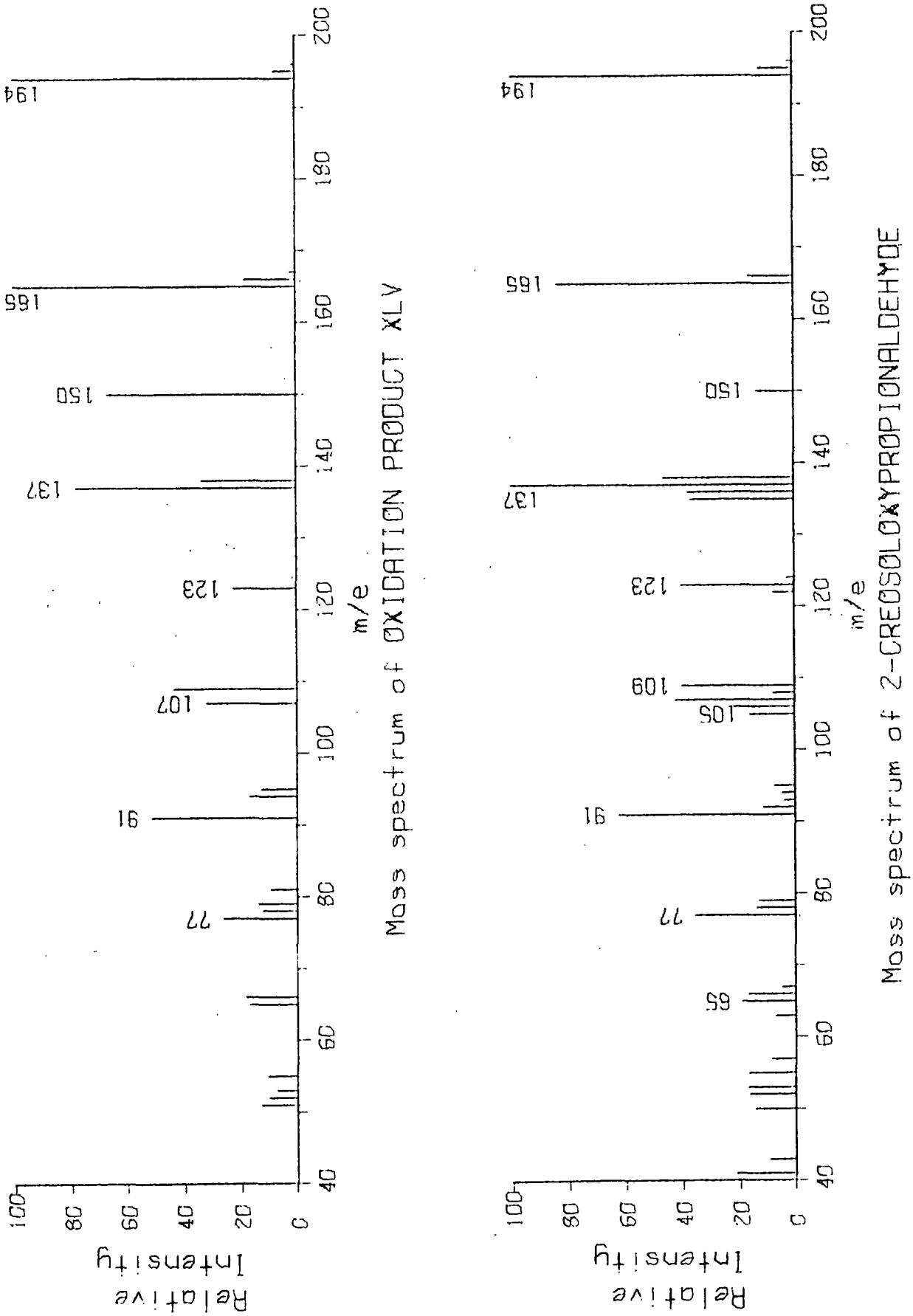
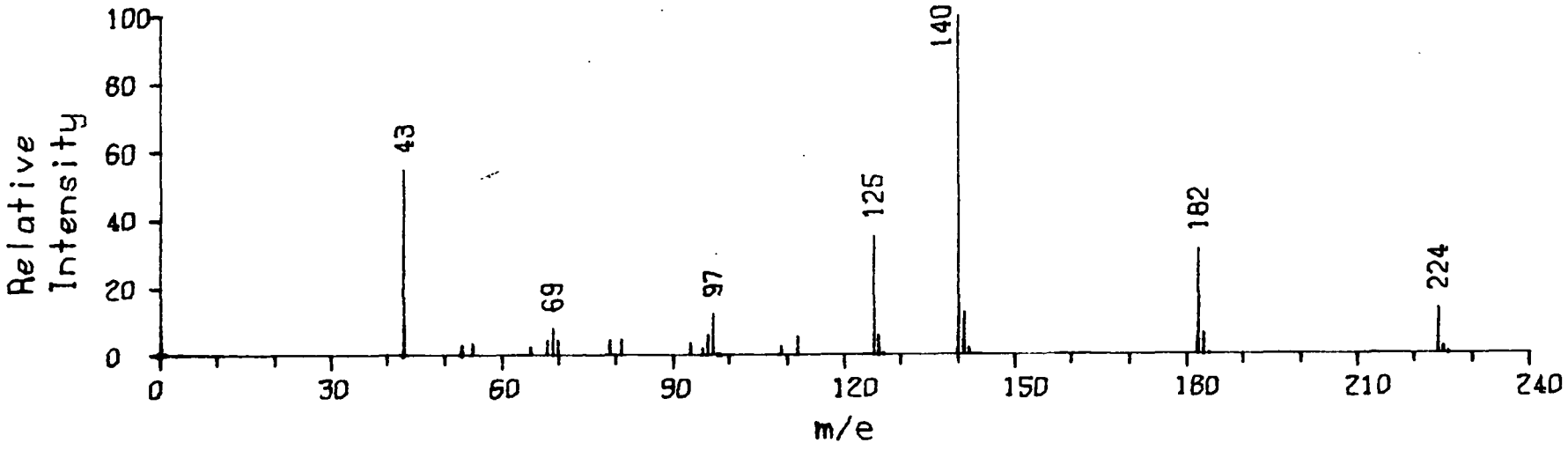


Figure 69. Mass Spectra of 2-Creosoloxypropionaldehyde and Oxidation Product XLV



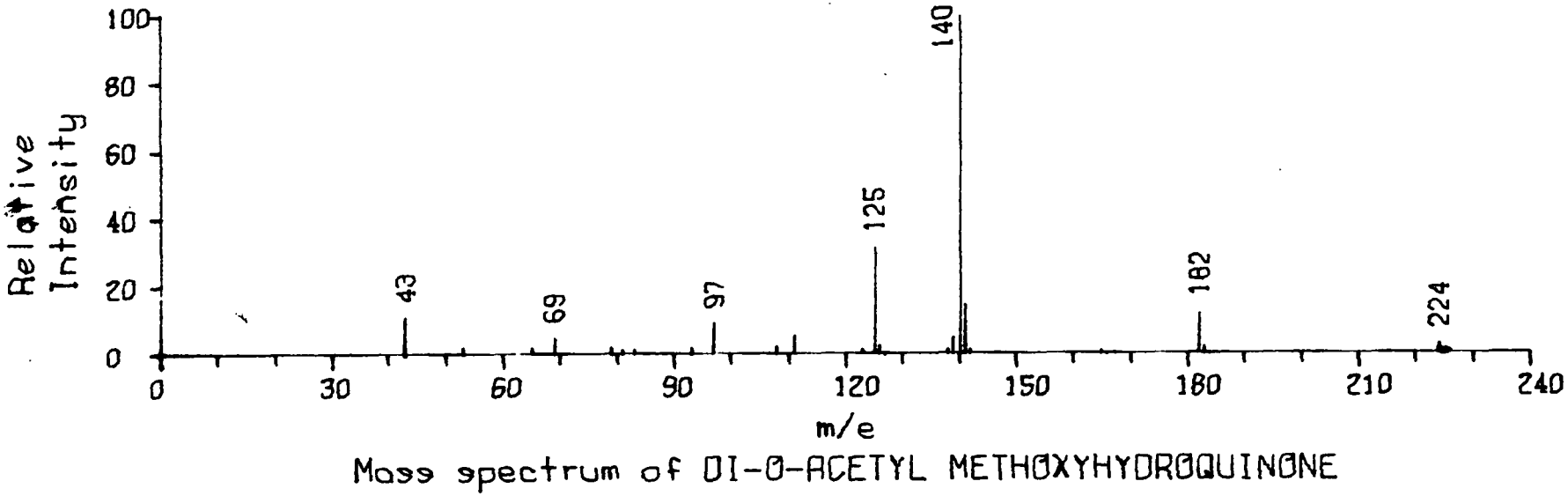
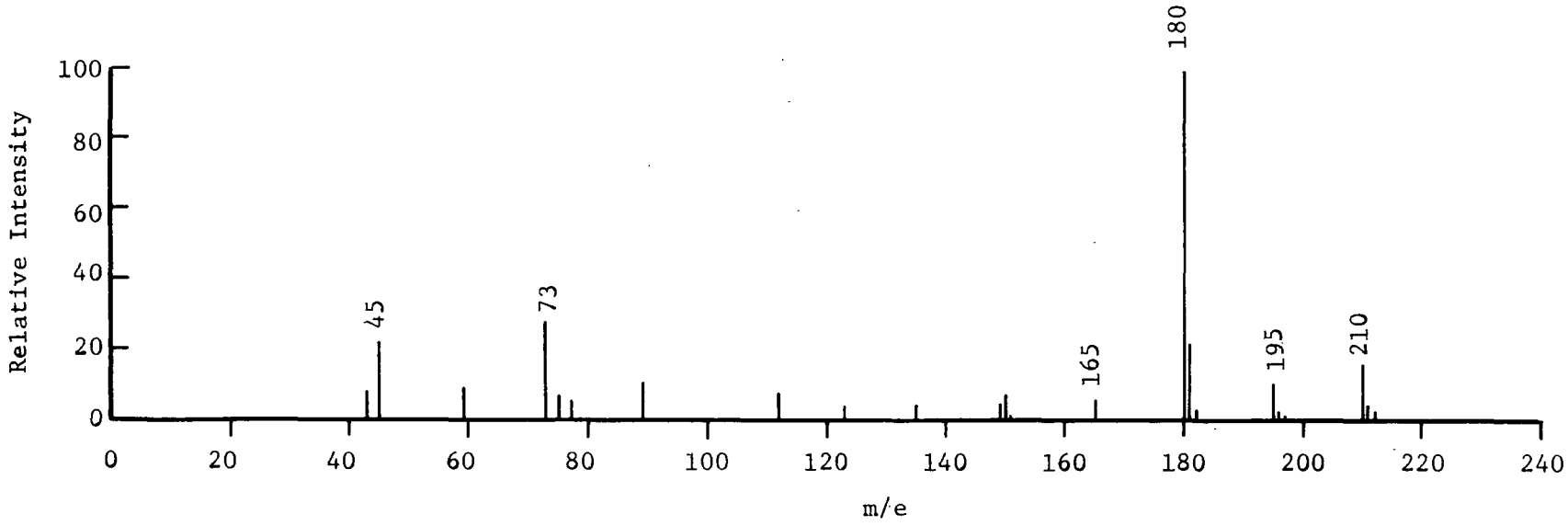
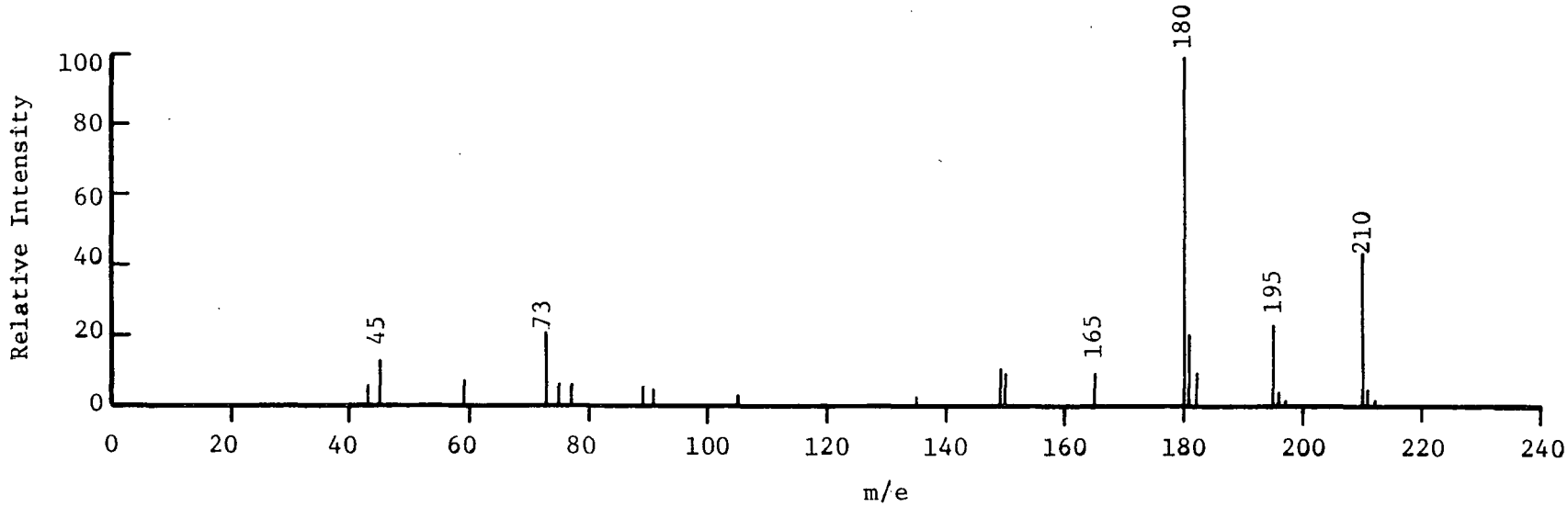


Figure 70. Mass Spectra of Di-O-acetylmethoxy-p-hydroquinone and Oxidation Product L



Mass spectrum of TMS ether of oxidation product LIV



Mass spectrum of TMS ether of creosol

Figure 71. Mass Spectra of TMS Ethers of Creosol and Oxidation Product LIV

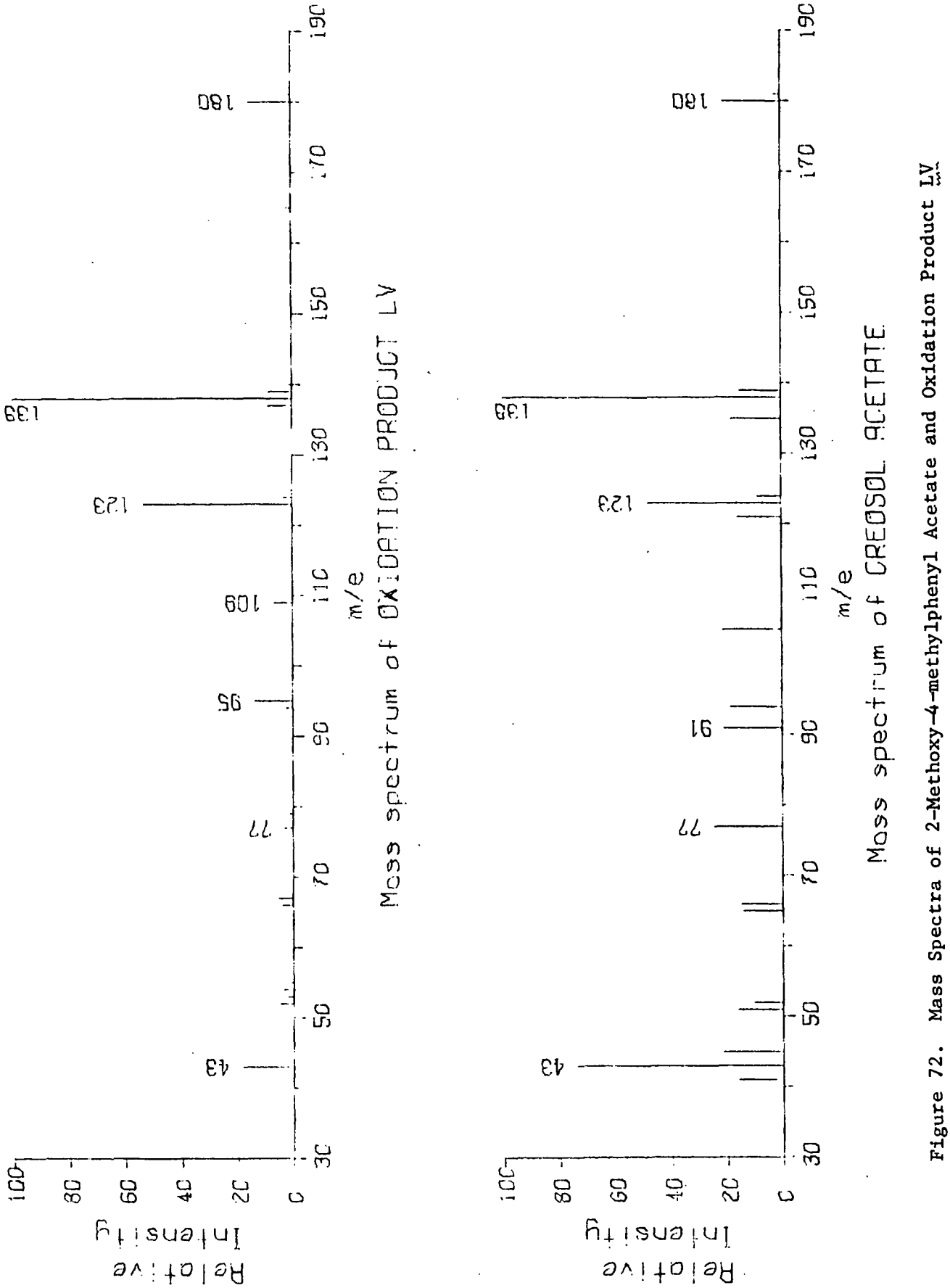
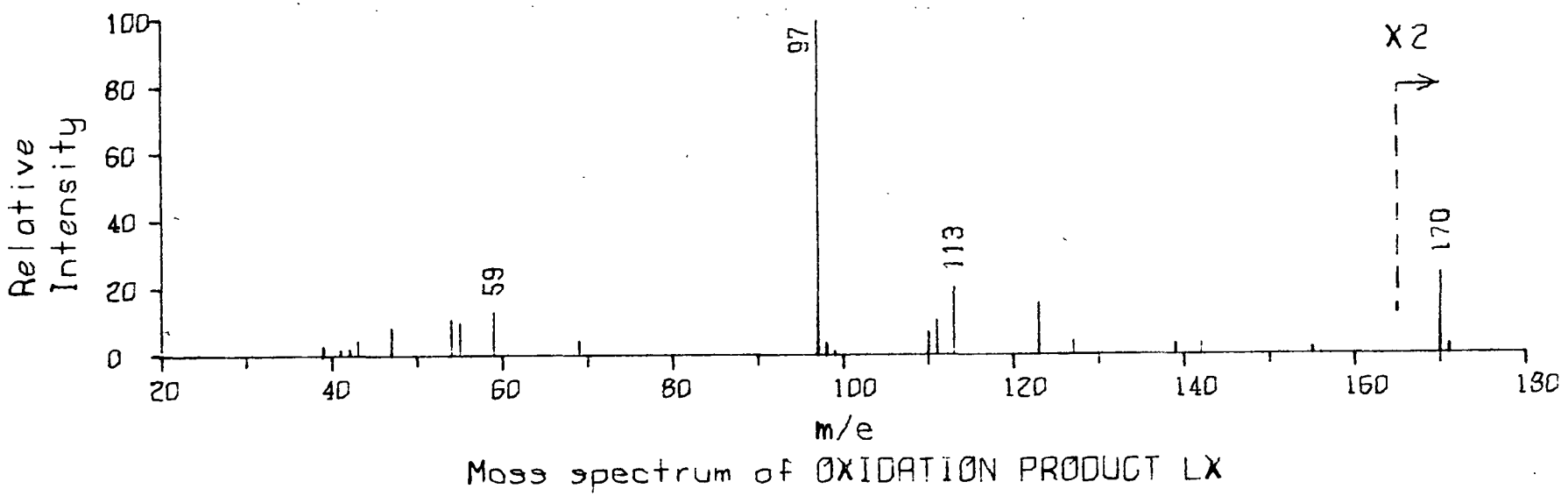


Figure 72. Mass Spectra of 2-Methoxy-4-methylphenyl Acetate and Oxidation Product LV



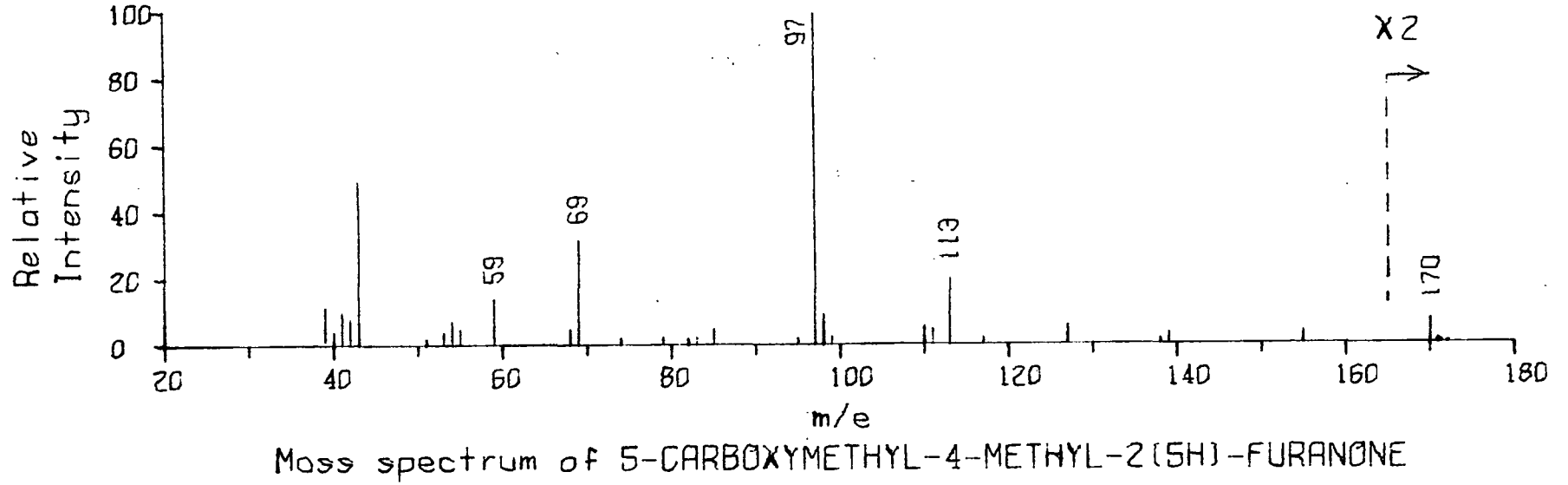
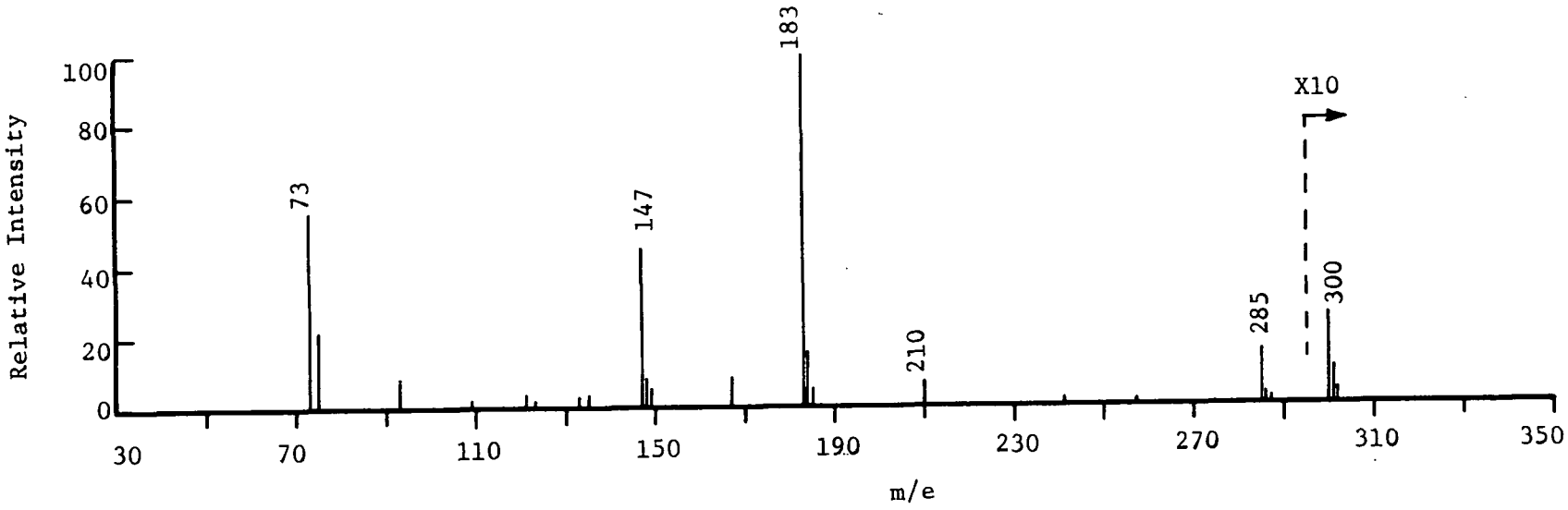
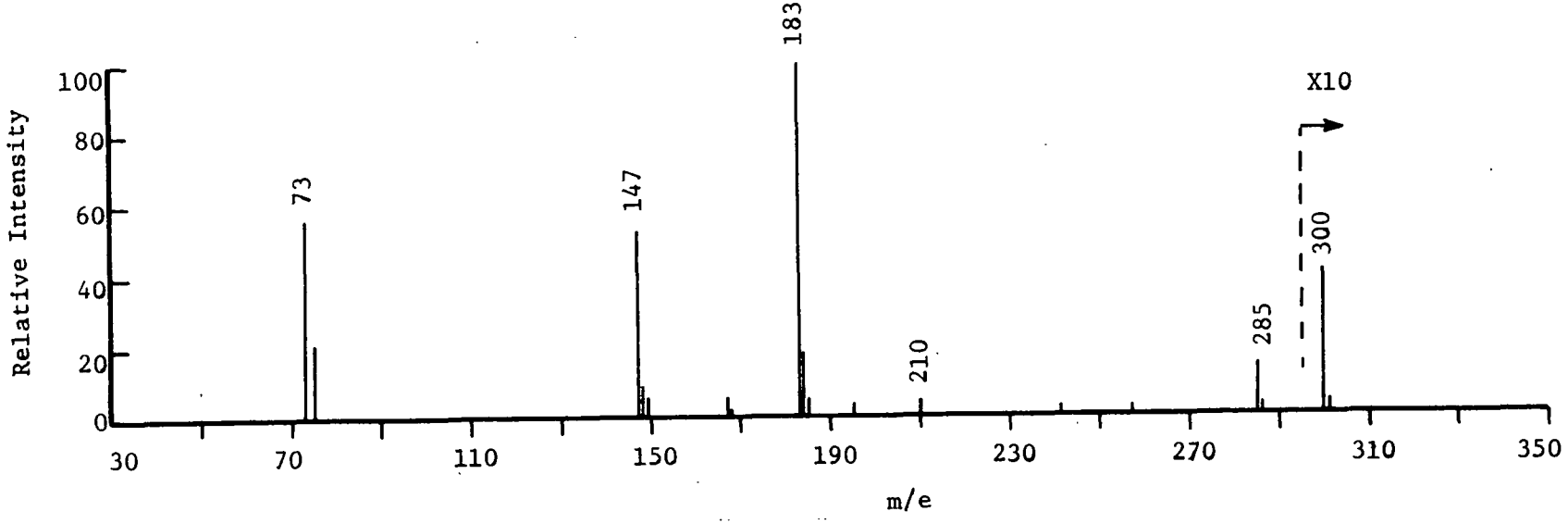


Figure 73. Mass Spectra of 5-Carboxymethyl-4-methyl-2(5H)furanone (19) and Oxidation Product LX



Mass spectrum of bis-TMS ester of oxidation product LXI



Mass spectrum of cis,trans-3-methylmuconic acid bis-TMS ester

Figure 74. Mass Spectra of bis-TMS Esters of cis,trans-3-Methylmuconic Acid and Oxidation Product LXI

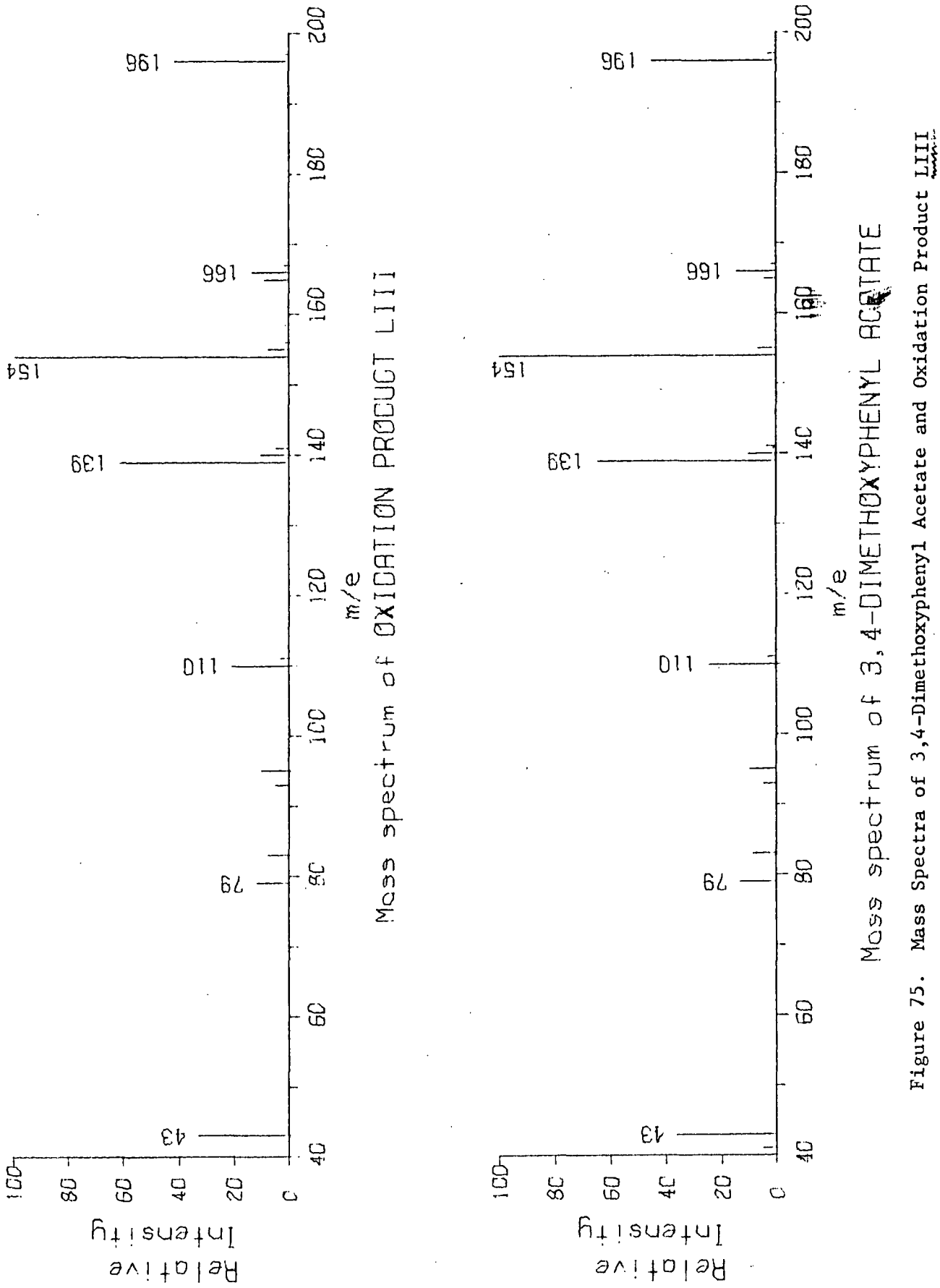


Figure 75. Mass Spectra of 3,4-Dimethoxyphenyl Acetate and Oxidation Product LIII

APPENDIX III

OXIDATION OF MODEL COMPOUNDS WITH PEROXYACETIC ACID

The data for calculation of percent reaction and stoichiometry for 1-(3,4-dimethoxyphenyl)-2-(2-methoxy-4-methylphenoxy)propanol, 1-(3,4-dimethoxyphenyl)-propan-1,2-diol, and 1-(3,4-dimethoxyphenyl)-1-hydroxypropan-2-one are given in Tables V-VII, respectively. Correction was made for decomposition of peroxyacetic acid. At the initial peroxyacetic acid concentration of 2.5%, control experiments showed this concentration to decrease by 0.002%/hour. Although the decomposition is not expected to be linear over the concentration range of the oxidation reactions (2.5-0.9%) this value was used for convenience.

TABLE V

DETERMINATION OF PERCENT REACTION AND STOICHIOMETRY FOR THE PEROXYACETIC ACID OXIDATION OF 1-(3,4-DIMETHOXYPHENYL)-2-(2-METHOXY-4-METHYLPHENOXY)PROPANOL

Time, hr	% PA[a]	% H_2O_2[a]	% PA_c[b]	[PA] x 10^3 mmoles/g	[β-E] x 10^3[e] mmoles/g	Δ[PA] x 10^3 mmoles/g	Δ[β-E] x 10^3 mmoles/g	Stoich.[d]	% Rxn.[e]
0	2.545	0.010	2.545	33.48	6.675	--	--	--	0.0
2	2.441	0.012	2.445	32.16	6.103	1.32	0.572	2.31	8.6
4	2.336	0.014	2.344	30.83	5.721	2.65	0.954	2.78	14.3
8	2.147	0.013	2.163	28.45	4.948	5.03	1.727	2.91	25.9
12	1.981	0.014	2.005	26.37	4.457	7.11	2.218	3.21	33.2
24	1.583	0.013	1.631	21.45	3.271	12.03	3.404	3.53	51.0
36	1.289	0.012	1.361	17.90	2.609	15.58	4.066	3.83	60.9
48	1.072	0.012	1.168	15.36	2.119	18.12	4.556	3.98	68.3

[a] % Peroxyacetic acid (PA) and H_2O_2 determined by method described in the Experimental Section.

[b] Corrected % PA based on correction factor given on page 138.

[c] Concentration of starting material based on determination by gas chromatography.

[d] Stoichiometry — moles PA consumed/moles substrate consumed.

[e] Percent of substrate reacted at time listed.

TABLE VI

DETERMINATION OF PERCENT REACTION AND STOICHIOMETRY FOR THE PEROXYACETIC ACID OXIDATION OF 1-(3,4-DIMETHOXYPHENYL)PROPAN-1,2-DIOL

Time,[a] hr	% PA[b]	% H_2O_2[b]	% PA_c[c]	[PA] x 10^3 mmoles/g	[VP] x 10^3[d] mmoles/g	Δ[PA] x 10^3 mmoles/g	Δ[VP] x 10^3 mmoles/g	Stoich.[e]	% Rxn.[f]
0	2.497	0.013	2.497	32.85	6.590	--	--	--	0.0
2	2.427	0.015	2.431	31.97	6.000	0.88	0.590	1.49	9.0
4	2.320	0.017	2.328	30.62	5.943	2.23	0.647	3.45	9.8
8	2.148	0.016	2.154	28.33	5.708	4.52	0.882	5.12	13.4
12	1.998	0.013	2.022	26.60	5.288	6.25	1.302	4.80	19.8
24	1.603	0.014	1.651	21.72	4.316	11.13	2.274	4.89	34.5
48	1.124	0.015	1.220	16.05	3.335	16.80	3.255	5.16	49.4
60	0.939	0.013	1.059	13.93	3.226	18.92	3.364	5.62	51.0

[a] Time after addition of peroxyacetic acid to reaction flask.

[b] % Peroxyacetic acid (PA) and H_2O_2 determined as outlined in Experimental Section.

[c] Concentration of substrate determined by gas-liquid chromatography.

[d] PA correction factor given on page 138.

[e] Stoichiometry — moles PA consumed/moles substrate consumed.

[f] Percent of substrate reacted at time listed.

TABLE VII

DETERMINATION OF PERCENT REACTION AND STOICHIOMETRY FOR THE PEROXYACETIC ACID OXIDATION OF 1-(3,4-DIMETHOXYPHENYL)-1-HYDROXYPROPAN-2-ONE

Time,[a] hr	% PA[b]	% H_2O_2[b]	% PA[c]	PA x 10^3 mmoles/g	VA x 10^3[d] mmoles/g	PA x 10^3 mmoles/g	VA x 10^3 mmoles/g	Stoich.[e]	% Rxn.[f]
0	2.597	0.015	2.597	34.16	6.633	--	--	--	0.0
1	2.196	0.016	2.198	28.91	3.942	5.25	2.691	1.95	40.6
2	1.984	0.013	1.988	26.15	2.410	8.01	4.223	1.90	63.7
4	1.720	0.014	1.728	22.73	1.100	11.43	5.533	2.07	83.4
8	1.458	0.016	1.474	19.39	0.319	14.77	6.314	2.34	95.2
12	1.282	0.013	1.306	17.18	0.133	16.98	6.500	2.61	98.0
24	0.971	0.012	1.019	13.40	0.014	20.76	6.619	3.14	99.8

[a] Time after addition of peroxyacetic acid to reaction flask.

[b] % Peroxyacetic acid (PA) and H_2O_2 determined as outlined in Experimental Section.

[c] PA correction factor given on page 138.

[d] Concentration of substrate determined by gas-liquid chromatography.

[e] Stoichiometry — moles PA consumed/moles substrate consumed.

[f] Percent of substrate reacted at time listed.

APPENDIX IV

CONCENTRATION AND YIELD OF OXIDATION PRODUCTS OF PEROXYACETIC ACID OXIDATION OF MODEL COMPOUNDS

The yields of the peroxyacetic acid oxidation products of 1-(3,4-dimethoxyphenyl)-2-(2-methoxy-4-methylphenoxy)propanol are given in Table VIII. The yield of 3,4-dimethoxyphenol in the peroxyacetic acid oxidation of 1-(3,4-dimethoxyphenyl)-1-hydroxypropan-2-one are given in Table IX.

TABLE VIII

CONCENTRATION AND YIELD OF PEROXYACETIC ACID OXIDATION PRODUCTS OF 1-(3,4-DIMETHOXYPHENYL)-2-(2-METHOXY-4-METHYLPHENOXY)PROPANOL

Time,[a] hr	LXI[b]		LIV[b]		XLa[b]		XLb[b]		XLI[b]		XLII[b]	
	Conc.[c]	Yield[d]	Conc.[c]	Yield[d]	Conc.[c]	Yield[d]	Conc.[c]	Yield[d]	Conc.[c]	Yield[d]	Conc.[e]	Yield[d]
2	N.D.		3.81	6.7	11.96	20.9	1.06	1.9	0.91	1.6	1.00	1.7
4	2.20	2.30	8.11	8.5	18.32	19.2	1.78	1.9	1.92	1.8	3.30	3.5
8	3.09	1.79	10.18	5.9	28.70	16.6	3.13	1.8	2.87	1.6	0.75	0.4
12	7.06	9.98	9.98	4.5	34.59	15.6	3.56	1.6	2.96	1.3	0.60	0.3
24	29.80	8.75	15.77	4.6	46.07	13.5	6.36	1.8	4.00	1.2	1.40	0.4
36	35.56	8.75	16.52	4.0	49.83	12.2	8.16	2.0	4.01	1.0	0.69	0.2
48	51.42	11.26	17.78	3.9	51.86	11.4	8.40	1.8	8.76	1.9	0.52	0.1

[a] Time after addition of peroxyacetic acid to reaction flask.

[b] Structure of product given in Fig. 16.

[c] Concentration in mmoles/g x 10^4; response factor determined.

[d] Yield given is percent of theoretical.

[e] Concentration in mmoles/g x 10^4; assumed response factor of 1.

TABLE VIII (Continued)

CONCENTRATION AND YIELD OF PEROXYACETIC ACID OXIDATION PRODUCTS OF 1-(3,4-DIMETHOXYPHENYL)-2-(2-METHOXY-4-METHYLPHENOXY)PROPANOL

Time,[a] hr	XLV + XLVII[b]		XLVII + XLIX[b]		XLIV[b]		LV[b]		L[b]		LVIII + LIX[b]	
	Conc.[c]	Yield[d]	Conc.[c]	Yield[d]	Conc.[c]	Yield[d]	Conc.[c]	Yield[d]	Conc.[c]	Yield[d]	Conc.[c]	Yield[d]
2	1.63	2.9	0.3	0.6	0.11	0.19	0.10	0.18	0.69	1.2	0.48	0.84
4	4.14	4.3	0.8	0.8	0.22	0.23	0.29	0.30	1.20	1.3	0.90	0.94
8	2.61	1.5	1.9	1.1	0.11	0.06	0.13	0.08	2.35	1.4	1.11	0.64
12	2.71	1.7	2.8	1.2	0.38	0.17	0.94	0.42	1.40	0.6	1.16	0.52
24	2.26	0.7	4.1	1.2	0.62	0.18	0.74	0.22	1.83	0.5	1.32	0.39
36	1.80	0.4	7.0	1.7	0.45	0.11	0.80	0.20	2.24	0.6	2.15	0.53
48	1.83	0.4	3.4	0.7	N.D.	N.D.	0.40	0.09	3.43	0.8	0.92	0.20

[a] Time after addition of peroxyacetic acid to reaction flask.

[b] Structure of product given in Fig. 16.

[c] Concentration in mmoles/g x 10^4; assumed response factor of 1.

[d] Yield given is percent of theoretical.

TABLE IX

CONCENTRATION AND YIELD OF 3,4-DIMETHOXYPHENOL IN THE PEROXYACETIC ACID OXIDATION OF 1-(3,4-DIMETHOXYPHENYL)-1-HYDROXYPROPAN-2-ONE

Time[a], hr	Concentration[b]	Yield[c]
1	2.4	8.9
2	13.6	32.2
4	29.4	53.1
8	35.8	56.7
12	30.4	46.8
24	17.7	26.7

[a] Time after addition of peroxyacetic acid to reaction flask.

[b] Concentration in mmoles/g x 10^4; assumed response factor of 1.

[c] Yield given is percent of theoretical.